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PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY,
OTOLOGY, RHINOLOGY, LARYNGOLOGY,
HYGIENE, AND OTHER TOPICS OF INTEREST
TO STUDENTS AND PRACTITIONERS

BY LEADING MEMBERS OF THE MEDICAL PROFESSION
THROUGHOUT THE WORLD

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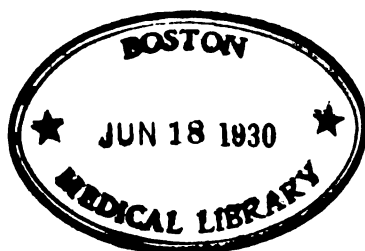
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Treatment

THE THERAPEUTIC USES OF THE RÖNTGEN RAYS, OR RADIOTHERAPY

BY GEORGE C. JOHNSTON, M.D.

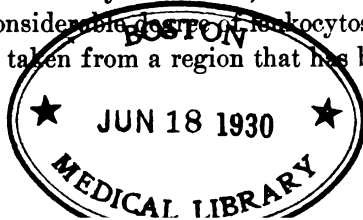
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THE employment of the Röntgen rays as a therapeutic agent was begun in a purely empirical manner, following several years of increasing use for diagnostic purposes. In order that their mode of acting may be understood, some conception of their physiologic action is requisite. The popular conception of this physiologic action is, that it consists merely of a burning, analogous to that produced by the application of heat, that it produces its therapeutic results by burning out the diseased tissue like the actual cautery or caustic, and that it cannot affect a pathologic process situated beneath the skin without, in so doing, affecting or destroying the skin itself. This erroneous idea is not confined to the laity, but is entertained also by many physicians well informed upon other medical matters. Others seem to consider the effects produced by the x-rays as electric in character, and, therefore, in common with electricity in every form, to be condemned as a remedial agent. A consideration of the facts in the case, however, will, I believe, serve to convince one of the fallacy of these beliefs.

PHYSIOLOGIC ACTION OF THE RÖNTGEN RAYS

When animal tissue is exposed for certain periods to strong radiation a peculiar series of phenomena occurs in it. If a section of skin, which has been exposed to sufficient radiation to produce decided reaction, be examined microscopically, there will be found the evidences of an ordinary dermatitis, with some dilatation of the capillaries and a considerable degree of leukocytosis.

If a section be taken from a region that has been submitted to a



course of radiation and is exhibiting macroscopically the evidences of atrophic change, a characteristic series of changes will be observed: The entire skin is thickened, especially in the Malpighian layer; the hair follicles have almost entirely disappeared; the papillæ are destroyed; and the sudoriferous and sebaceous glands have disappeared. If the skin be pigmented, the pigment will be found to be deposited in the papillæ and the outer layer of the cutis. Marked changes in the walls of the blood-vessels are present and are almost analogous to those seen in obliterating endarteritis. Frequently masses of cells are seen occluding the lumen of the small vessels. These are evidences of the response of the skin to a severe degree of irritation, and this is just what prolonged radiation amounts to.

A great many studies have been made of the various effects of x-rays upon tissue, and most observers agree in their findings. It may be said in general that x-rays, when applied for a considerable length of time to a part, affect the cellular elements of the skin in such a way as to give rise to the slow degeneration described above. The glandular elements of the skin are the next to suffer, undergoing a slow atrophy that results in complete disappearance of these elements, with no attempt at replacement. An increase in connective tissue occurs, similar to that following inflammation from any other cause. The nerves and large blood-vessels, muscles, ligaments, cartilage, and bone, suffer only secondarily, and to the greatest degree in those severe cases characterized by extensive destruction of tissue. In cases of reaction following treatment with radiation of high penetration, the evidences of violent inflammation are often manifested deeply by a profuse leukocytosis and by proliferation of connective tissue and atrophy of glandular structures. Thus, in carcinoma of the breast, which has been x-rayed before operation, the surgeon frequently encounters small, hard, fibroid masses of degenerated carcinomatous glands, with the underlying muscular structure matted firmly together by new-formed connective tissue, and the blood-vessels sometimes entirely obliterated, with thickened intima and surrounded by masses of leukocytes.

The changes taking place in pathologic tissue following radiation are most interesting, and have been studied thoroughly in lupus, sarcoma, and carcinoma. These changes seem to consist of the rapid degeneration of the pathologic tissue-cells, followed by their absorp-

tion, and the replacement of such cells by normal connective-tissue cells, which shortly contract and lead to some apparent atrophy of the site of disease. The degree and character of the degeneration following the exposure vary greatly with the technic employed. In some cases this degeneration has much in common with ordinary fatty degeneration. In other cases a fibro-myxomatous or colloid change may be observed. These phenomena may follow a single prolonged exposure, or may be manifest only after a number of exposures.

The degree of the reaction following is determined by several factors, such as the length of exposure, the distance from the tube, the vacuum of the tube, the intensity of radiation, the number and intervals between exposures, etc. This reaction is known as an x-ray dermatitis, and if very severe is often termed a "burn." It varies from a simple erythema, with a little subsequent tanning, to a veritable slough of the cutis and subcutaneous tissue.

The erythema follows the exposure at an interval of from a few hours to several days, is attended by local rise of temperature and formication, subsides in a few days, and is followed by a slight irregular desquamation.

In more severe cases (second degree) the onset is similar, but the erythema is followed by intense burning, itching, and vesiculation; the vesicles if undisturbed dry up, and upon the separation of the crusts a new growth of epithelium is found,—very delicate, bleeding easily, and quite sensitive. This rapidly hardens and the parts regain a normal appearance, save for some slight degree of tension in the new skin.

In still more severe cases (third degree) the vesicles become pustular. Repeated attempts at healing are made, but the tissue only breaks down again. Finally, a rough necrotic ulcer, with a hard, raised, inflamed border, is formed. This may persist for years, making little, if any, attempt at repair, and becoming possessed of every new and old variety of painful sensation, out of all proportion to the area involved, worse at night, and resisting all attempts at treatment short of wide excision. These so-called x-ray burns were rather frequent in the early x-ray work, and were usually the result of exceedingly long exposures necessitated by the inefficient apparatus obtainable at that time.

A consideration of the pathologic results following this radiation

suggested the possibility that an agent having the power of producing such changes in healthy tissue might be used to advantage in the treatment of some of the more chronic forms of skin lesions which had shown themselves to be benefited by deep inflammation induced by other means. The experiments proving successful, it was extended by the investigators to include the various forms of superficial malignant growths, especially those of slow progress and small degree of malignancy, such as epithelioma of the face. The results were so satisfactory, in some instances such apparently wonderful results were obtained, that the more enthusiastic investigators began to announce the x-ray as a panacea for every form of malignancy. A few years of harsh experience has abundantly disproved this claim, but it has reduced radiotherapy to an exact basis, and upon this basis it has settled itself as a valuable and accepted therapeutic agent.

TECHNIC OF RADIOTHERAPY

Success in radiotherapy depends upon the ability of the operator to administer a known dose of x-rays at such intervals as each case may require. There is no one thing or instrument that will measure the quality and quantity of x-rays given off from a tube at any time. The experienced operator judges this by a combination of factors, each of which he has learned to observe. Meters in the primary circuit measure the amount of current passing through the primary circuit winding. Meters in the secondary circuit measure the volume of current passing through the tube. Each tube may be looked upon as a transformer. Here a high tension, practically unidirectional current, is transformed into x-rays, heat, etc. No meter can be a measure of the efficiency of such a transformer, but simply of the load it is carrying, and of the vacuum and resistance of the tube. Naturally, a given electromotive force will drive more current through a low tube than a high one.

The only way in which a standard dose can be formulated is for the operator to balance all the different factors constituting such a dose.

Interrupters.—It has been my experience that the form of interrupter used in treatment determines the dosage to a considerable extent. The Wehnalt interrupter, when used on the alternating current, being prone to great variations, requires considerable watchfulness to regulate the excitation of the tube. The vibrator or the

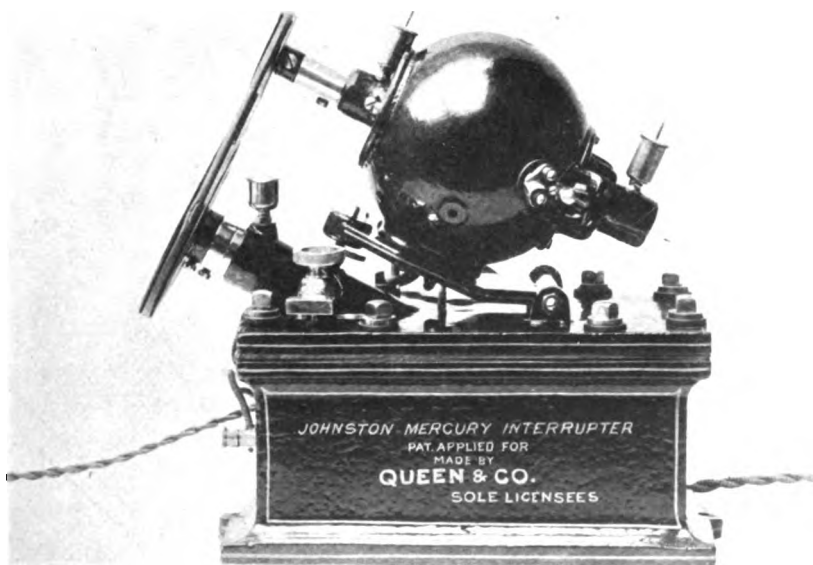
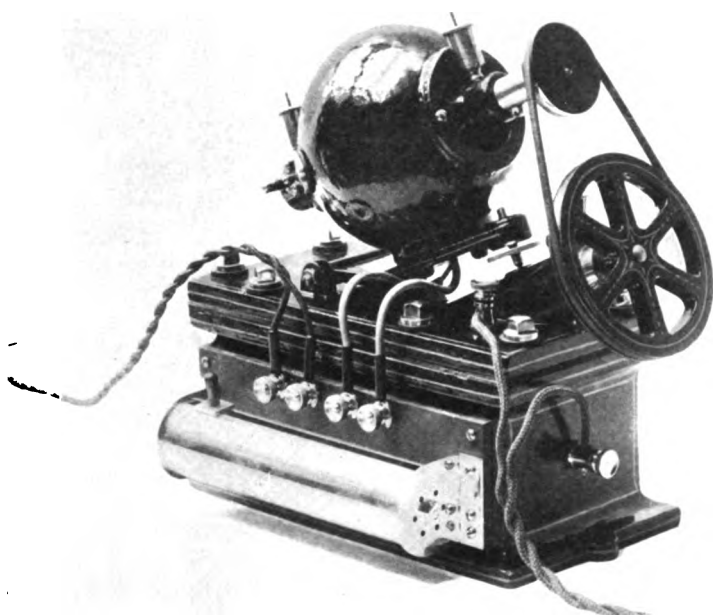


FIG. 1.—The author's mercury interrupter, used exclusively in his therapeutic work.

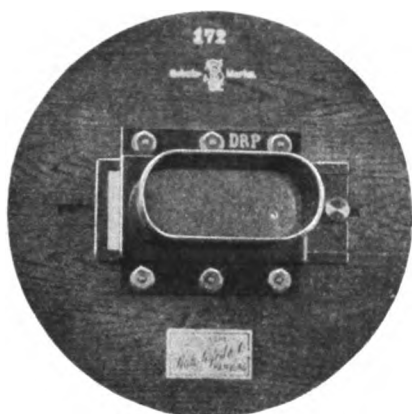


FIG. 2.—Walter skiameter, or fluorometer, for indicating the penetration of the radiation of an x-ray tube.

mercury dips (Fig. 1) is the most preferable form of interrupter for therapeutic use. The winding of the coil influences the dosage; thus, a 15-inch coil with a single winding may require three times as much current in the primary coil to produce the same secondary output as another 15-inch coil having a series winding of the primary coil. In the same way the size of the coil must be considered. It is not advisable to use a coil smaller than 12 inches for therapeutic works.

Spark-Gaps.—Introduction of one breaker or a series of breakers in the secondary circuit has been found to have certain definite effects upon the operation of the tube: (1) The penetration of the rays given off is increased; (2) the heating of the tube is decreased; and (3) the inverse discharge is diminished or suppressed.

Penetration.—The penetration of the radiation from a given tube depends to a certain degree upon the resistance and the state of vacuum of the tube. This penetration must naturally be determined either by a suitable penetrometer, such as the Walter fluorometer (Fig. 2), or by examination by the operator of the body of a patient. The hand, which is the natural penetrometer, must not be used for this purpose, as this habit is responsible for the condition of the hands of some of the best known x-ray operators. In the Walter penetrometer a thick lead screen is penetrated by a series of holes. These holes contain each a different thickness of platinum foil. Over the lead plate is placed a small fluorescent screen provided with a suitable eye-piece. Upon holding the fluorometer at a given distance from the excited tube, the radiation will be found to penetrate the platinum foil in proportion to its thickness, and passing through the foil will render the screen more or less fluorescent. The observer sees a series of round spots illuminating in a decreasing ratio from number 1 upward; thus the rating W 5 indicates that a certain tube at the standard distance gives off rays of sufficient penetration to illuminate the screen through the thickness of platinum up to and including the fifth hole.

These penetrometers are standardized only so far as the thickness of the platinum covered holes is concerned. The reading of such a penetration introduces a variable personal equation; thus the observer, if previously in a darkened room for a few minutes, will read a much higher penetration from the tube than one whose eyes have not become accustomed to the darkness. He will read a lower

penetration when a tube is operated in an illuminated room. He will read a higher or lower penetration depending upon whether the fluorometer is drawn toward or away from the tube. As the screen grows older the reading must grow less—whence it cannot be looked upon as even approximately correct; but such an instrument will enable the operator to judge his own tube in conformity with his own ideas of penetration.

The penetration of the tube will be found to bear a certain relation to the length of the spark-gap in air against which the resistance of the tube just balances. Usually the longer this gap, the higher the vacuum of the tube and the more penetrating the radiation therefrom, but very many tubes will be found in which this rule does not hold even approximately good.

Focus.—The closely focussed tube is not especially desirable for therapeutic use, but should rather be reserved for radiography. Such a tube will be found to be much more active at the central portion of the area exposed to radiation than at the periphery; if used it must be shifted at each exposure in order to balance the effect.

Tube Distance.—X-rays, in common with all forms of radiation proceeding from a point, fall off as the square of the distance; thus, if the distance from the anode of the tube to the surface of the lesion be in one instance 8 inches, and in another 16 inches, or twice the distance, the amount of radiation received at any given point in the second case will be not one-half as great, but one-fourth as great. This must be constantly borne in mind if uniform results are to be obtained.

Moreover, this same fact has a most important bearing upon the success attending the treatment of lesions lying at a considerable depth below the surface. Thus, supposing the anode of the tube be placed at a distance of 8 inches from the surface of a breast containing a carcinoma which extends 4 inches below the surface of the skin, then the distance from the anode to the surface is, as stated, 8 inches, and the distance from the anode to the farthest portion of the tumor is 11 inches. Now, the amount of radiation received by any point upon the surface of the skin in a given length of time may be stated as 64 units (the square of the distance 8 inches), and the square of the distance of the most remote portion is 121; therefore, at any point lying in the plane there would be received from the same tube, in the same length of time, under the same conditions,

$\frac{64}{121}$ as much, or practically one-half as much. The result of continued treatment of a lesion at such a tube distance must be over-radiation and possibly necrosis of the surface before the desired therapeutic effect has been obtained at the deepest portion of the growth. Thus, in treating a chest for tuberculosis, the variation in depth may be as great as 10 inches. By treating front and back alternately this may be divided when the greatest value is 5 inches.

Since this factor of depth is fixed and unchangeable, and it is desired to obtain practically equal values of radiation at the surface and at the greatest depth, we must change the value of the tube distance. If the tube were infinitely distant, the radiation at the surface and at the deepest point would have the same value. Since at such a distance the amount of radiation in both cases would be infinitely small, this is out of the question, but if the tube distance be increased to a relatively great distance,—for instance, 20 inches,—the variation in value of the radiation received at the surface and at the deepest point will be so small that it may be ignored. Since the radiation at both points has fallen off as the square of the tube distance, the amount of radiation received must be increased by increasing the time value, and the equation resulting may be expressed as follows:

Let d equal the distance from the surface under the usual exposure, 10 inches; let D equal the distance in the correct method, 20 inches; let t equal the time of exposure under the first condition, 10 minutes; and let T equal the required time of exposure under correct conditions. Then

$$d^2 : D^2 :: t : T$$

$$T = 40,$$

and a 40-minute exposure at 20 inches is equal to a 10-minute exposure at 10 inches, and affects the deeper tissues equally.

Duration of Exposure.—The length of exposure depends upon the capacity of the apparatus for exciting the tube. This capacity is such a variable quantity that it is impossible to formulate a time factor that will be more than approximately correct. It may be said, in general, as follows: For a static machine, having eight revolving plates at a speed of 300 revolutions per minute and a tube distance of 10 inches, the time of exposure should not exceed 15 minutes; four plates at 600 revolutions, or two plates at 1200 revolutions, will give about the same result. With a 15-inch coil, taking a primary

current of three amperes, and giving an output of 2.5 milliamperes, at a tube distance of 10 inches, an exposure of 7 minutes will be found suitable. Coils of small spark-length (7 to 8 inches) must not be rated in capacity according to the spark-length. Small special coils are often able to force a current through the resistance of the tube (until the resistance of that tube is greater than can be overcome by the total electromotive force of such a coil) which will be found upon measurement to equal in volume that of coils of much greater rated spark-length.

As a general rule, it is safe to estimate the amount of x-rays given off by the amount of heating of the anode of the tube. As a routine practice, and until such time as the operator has acquired a considerable amount of experience, it is best that he should not excite his tubes in treatment beyond the appearance of a red spot upon the anode. Such a tube, backing up a parallel spark in air of $3\frac{1}{2}$ inches, excited to the above degree, will be found therapeutically active.

Frequency of Treatment.—In my judgment the present tendency in radiotherapy lies toward over-treatment. A daily radiation with a moderately excited tube of high vacuum has, in my experience, shown a tendency toward irritation and stimulation of malignant processes in some instances. It is my preference to give on certain days definite doses of radiation of considerable magnitude, observing the effect of such radiation and repeating or withholding the dose, as indicated by the behavior of the tissue. As a general rule, treatment is not indicated oftener than every other day.

In beginning the treatment of a patient it is necessary to be on the alert for those who seem to possess a peculiar degree of sensibility or idiosyncrasy to radiation. If the patient be blonde and possessed of a brilliant complexion, frequently seen in those of a strumous diathesis, a few tentative treatments at intervals of several days are best undertaken. In the treatment of the various forms of skin lesions the most satisfactory results are found to follow interrupted series of treatments; thus, some ten treatments covering a month may be administered, some considerable degree of reaction obtained, and a rest be given the patient for a week or ten days, during which time the reaction disappears, and a large degree of the benefit to be derived from this series manifests itself. Treatment is then undertaken for another month, etc. In the treatment of deep-seated malig-

nant growths, such as carcinoma of the breast, such interruption is not usually called for.

Toxemia.—When a portion of the body of a patient is exposed to radiation from an excited Crooke's tube for a considerable period of time, or for a series of shorter periods aggregating some considerable time, pronounced change in the life processes of the cells constituting the part follow. More especially is this true if the radiation be directed against the part for a therapeutic purpose, such as the cure of a malignant process. Under such conditions there takes place (1) a marked irritation of the malignant tissue, and (2) a degeneration, even cell necrosis at times, a marked leukocytosis, and a choking of the area by newly-formed, rapidly propagating connective tissue cells. Now, if the growth has previously broken down the skin, if it be open and ulcerating and contain one or more sinuses, the cell necrosis may go on with impunity, the products of such necrosis being discharged externally in a sanious, odorless, purulent discharge. If, however, the growth be deeply seated, no matter how small it may be, the burden of eliminating the whole of the poisonous products of necrosis must fall upon the skin and the kidneys. If the patient is young, not overly fat, his kidneys competent, and his skin active, this may be accomplished by these organs, and the patient's general health may not suffer beyond, perhaps, some vague pains in the limbs, dull headache, coated tongue, and constipation.

If the temperature be taken under such conditions, an elevation of from 1 to 1.5° F. is usually observed. The urine will be heavy, with a specific gravity of 1020 to 1025, dark colored, and shows a considerable quantity of albumin. If the operator is on the watch for this condition, observes it early, stops radiation, gives his patient a free cathartic, and an abundance of the best diuretic, pure water, and perhaps a hot bath to stimulate the skin, the toxemia, for such it is, will not advance, but will slowly disappear. *Under no circumstances must any further radiation be given until the urine becomes normal, the tongue clean, and the lassitude and headache disappear.*

If the operator be inexperienced and ignorant, and does not read the plain danger-signals of impending intoxication, but continues to break down more tissue than the patient can eliminate, then, after a few days of malaise, the patient may send word that he is unable to report for treatment. Upon examination he will be found in bed

with the symptoms of a mild bronchitis, ammoniacal breath, and constipated; his urine is scanty, high colored, and loaded with albumin; his tongue dry and hard; his breath exceedingly foul; and he is dull, stupid, and complains of headache. In this condition the patient, if old and feeble, may develop a grave form of bronchitis and quietly die, the diagnosis in such cases being usually pneumonia.

Should the inactivity of the kidneys continue for three or four days, one would expect the ordinary train of uremic symptoms to manifest themselves, but I have no knowledge of any case in which this has occurred. The skin, fortunately, feels called upon to assist the kidneys, and in so doing suffers just as in the eruptive fevers. The degree of inflammation resulting from the vicarious elimination of these toxins by the skin must be seen to be believed. It is a most intense, desquamative, general dermatitis in which, as in the more grave forms of scarlatina, the skin covering the hands and feet is sometimes exfoliated in partial casts. In Fig. 3 is shown the skin covering the palm of the first patient in whom I observed this desquamation.

The size of the malignant growth under radiation at the time bears no relation whatever to the intensity and gravity of the toxemia induced. Dr. Alfred Stengel, in a conversation with me, expressed his belief that nothing short of cadaverin in all possibility possesses such a toxicity. This general dermatitis is attended by the most aggravating itching, and formication. The patient scratches himself until exhausted, leaving the skin bleeding and torn. The condition is usually diagnosed as an x-ray burn by practitioners who have never seen a similar case and who know that the patient has undergone a course of treatment. Each patient whom it has been my fortune to observe was given long-continued intense radiation of small, deeply-seated carcinomas of the lower lip. In each case, due, perhaps, to swallowing of the irritating and acrid discharge which streamed from the site of the sloughing growth, an alarming degree of edema of the posterior pillars of the fauces and of the larynx was present for several hours, but subsided under appropriate treatment.

The subject of toxemia as a result of over-radiation has not been discussed with sufficient freedom, the average writer being in considerably greater haste to report flattering achievements than to describe his unsuccessful cases. The treatment of toxemia may be

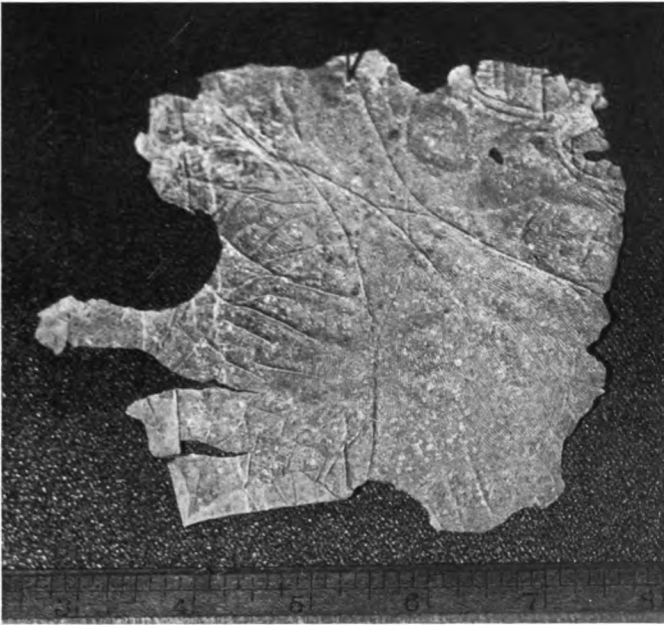


FIG. 3.—Skin of palm exfoliated in a case of toxic dermatitis following radiation of a small carcinoma of the lower lip in a patient of 60 years.

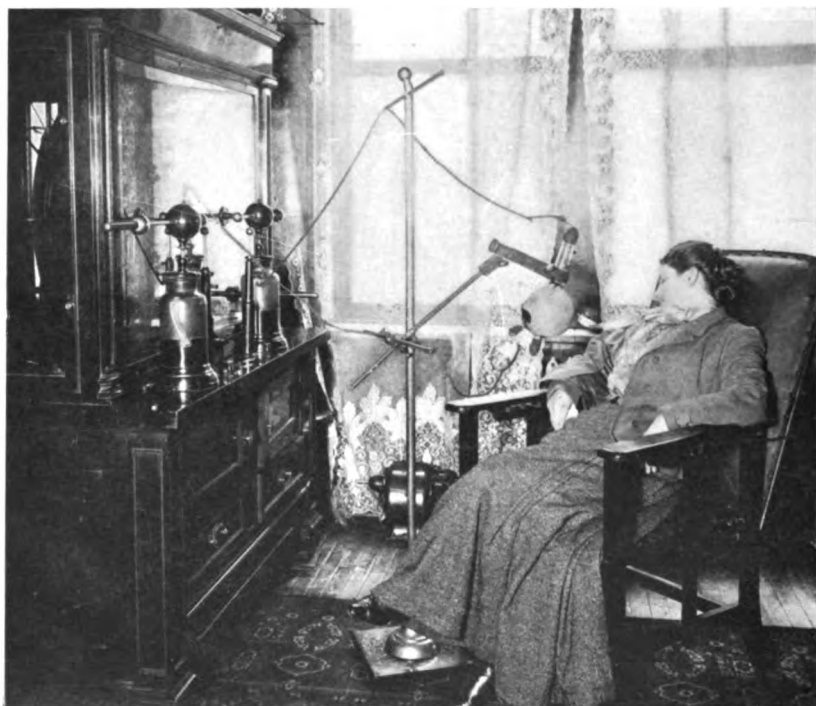
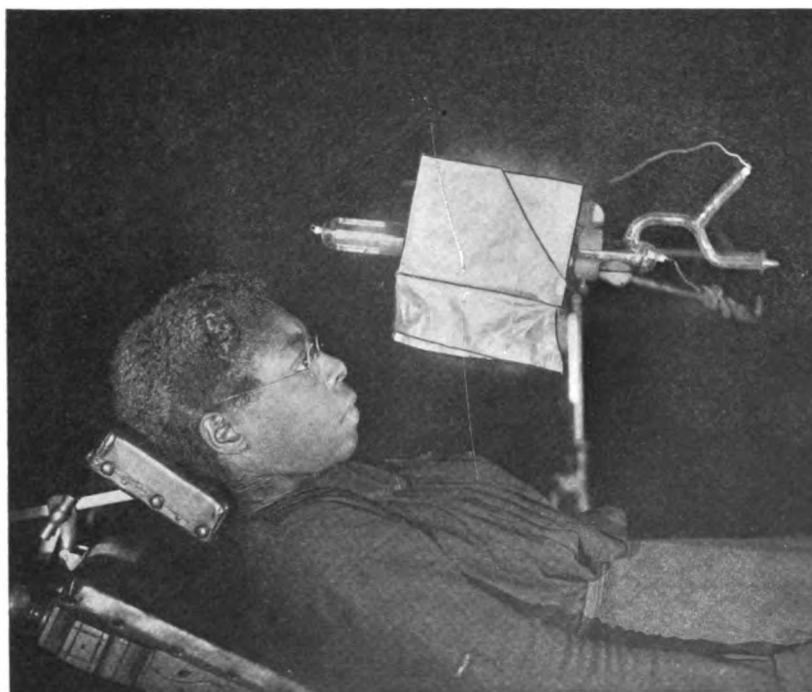


FIG. 4.—Tube-shield of rubber in use in the treatment of carcinoma of the breast.



FIG. 5.—The Friedlander tube-shield—protecting the operator and the patient.



**FIG. 6.—Pasteboard box covered with lead foil, for protecting the operator and localizing the x-rays.
Device of Dr. Leonard, of Philadelphia.**

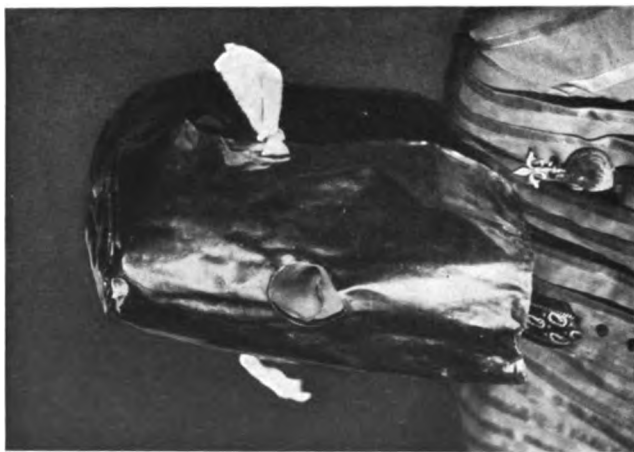


FIG. 7.—Lead mask applied in the treatment of lupus of the nose.

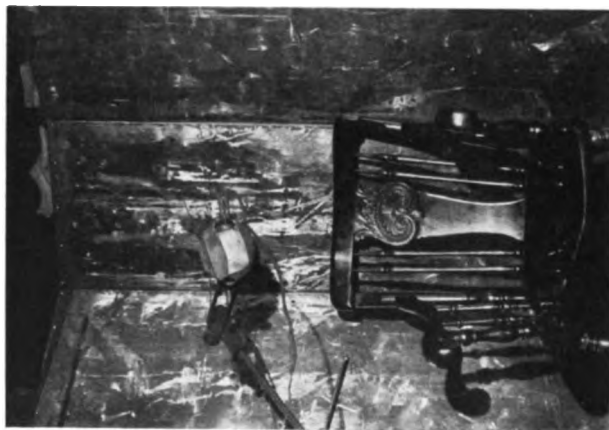


FIG. 8.—Adjustable lead screen for protecting the operator.

summed up in two words: "Avoid it." If a daily watch be kept upon the patient's tongue, the bowels kept active, and the ingestion of large quantities of water insisted upon, with a prompt suspension of radiation and administration of active eliminating treatment upon the approach of the preliminary symptoms already outlined, toxemia need not be dreaded.

Protection of the Patient.—It is usually necessary or desirable to protect from the action of the x-rays such portions of the body of the patient as are free from disease. This may be accomplished in a variety of ways. In Fig. 4 is shown a tube covered by a rubber coating impregnated with antimony, having a circular window opposite the anode, whereby a cone of rays is allowed to emerge from the tube. In Fig. 5 a useful form of tube-shield is shown, by which a localized area may be rayed with safety. The method of Dr. Leonard, of Philadelphia, for protecting the operator while localizing the rays upon the patient is shown in Fig. 6, the tube being placed in a pasteboard box, covered with heavy foil, having three curtains of foil which may be bent into any position, thus permitting the raying of varying areas.

In addition to these methods of shielding the tube, it is advisable to have at hand a quantity of lead foil impregnated with tin, and of sufficient thickness to be opaque to all but the heaviest forms of radiation. From this foil the operator, after a little experience, will be able to form masks to cover different portions of the body, in which windows may be cut considerably larger than the area of diseased tissue, so as to permit of the radiation of a considerable portion of surface beyond (Fig. 7). This is always wise practice. No malignant growth should ever be screened closely, as it is impossible for one to determine by external examination the exact limit of such growths, and a liberal safety factor must be supplied by raying wide of the apparent limit of disease.

Care should be taken when possible to avoid the loss of hair by protecting the scalp by a suitable screen, unless a shielded tube is used. While the epilation effected by x-rays is usually transitory, yet, if the treatment be prolonged, the result may be permanent. The use of x-rays for purposes of epilation for cosmetic effect is certainly not to be recommended, except in cases in which the hair is so thick and coarse as to constitute marked disfigurement. The use of x-rays for ordinary epilation is about as justifiable as the

administration of a general anesthetic for the extraction of a few milk teeth.

In every case of malignant disease a number of treatments should be given *without any protective screens whatever*, in order to influence any suspected tissue as far distant from the original growth as possible.

Protection of the Operator.—The majority of men who have done much x-ray work are suffering at the present from the immediate or remote effects of constant exposure in the x-ray field. This is partly the result of early ignorance and, in some cases, a contemptuous disbelief in their liability to such results. The hands of the average radiographer are an indication of his vocation. The destroyed and rudimentary nails, the discolored ulcerations and keratoses, the red, tense, shiny skin, and the absence of hair, bear evidence of a chronic inflammation and atrophic degeneration of the skin and its appendages. The use of the fluoroscope in diagnostic work, so prevalent some years ago, and still followed by those whom experience has yet to teach, was and is responsible for a great deal of this, but there are other deleterious effects of constant exposure, either to the radiation from the excited tube itself or from the radioactivity of metallic and other objects in the vicinity of the tube, which have a direct effect upon the general health of the operator, and must be avoided when possible.

The following rules of conduct are prophylactic against such results: (1) Remain in the treatment room no longer than necessary properly to arrange the patient and tube and begin operation. If the operator's presence in the room is necessary, let him remain behind a large screen suitably upholstered and covered with lead of a weight of at least $2\frac{1}{2}$ pounds to the square foot; such a screen will be found to be opaque to practically all x-rays (Fig. 8).

(2) Wherever possible use all treatment tubes only in conjunction with one of the forms of tube-shield illustrated.

(3) During treatment the operator should remain in an adjoining room where he can hear the operation of his apparatus. If a reliable regulating x-ray tube only be used for therapeutic purposes the vacuum will remain practically constant. The apparatus to excite the tube must be of a form that, once started, will deliver a constant and uniform secondary discharge for the operation of the tube without the supervision or presence of the operator. All tubes at all

times must be so placed with reference to the retiring room that the radiation shall be cast in a direction away from the operator.

(4) When examining the relative position of the tube and patient, or making adjustments of any kind, always shut off the current from the tube.

(5) Do not allow yourself to be used as an exhibition of the penetration of the x-rays.

(6) In testing the vacuum of tubes employed use a fluorometer, *not the hand*.

If these precautions be followed, there will be no more distressing cases of chronic, even malignant, dermatitis.

RADIOTHERAPY IN DISEASES OF THE SKIN

Sycosis.—The value of radiation in the various forms of sycosis is due, not only to its depilatory effect, but also to the fact that, aside from any direct germicidal powers which it may have, the inflammation resulting from its application renders the tissues decidedly unfit for the growth of the various microorganisms responsible for sycosis. The depilation is painless and complete, and were this the only effect obtained by radiation, such treatment would more than repay one for the time and trouble expended.

In the treatment of sycosis, as in the treatment of all skin diseases, it is necessary to proceed cautiously. A very soft tube should be used at a distance of at least 8 inches, and treatment should be interrupted at the first sign of reaction. It is often advisable at least to decrease the frequency of the treatments as soon as blanching and loosening of the hair appear. Under no circumstances should the application of the customary remedial agents be neglected.

Results in sycosis are obtained by cautious treatment. A burn is to be avoided, and the hair follicles should be preserved intact, if at all possible. A pronounced dermatitis will often be followed by relief from the sycosis, but at the expense of the hair.

The actual value of x-ray-therapy in this troublesome skin lesion has been demonstrated by many operators.

The following cases illustrate the technic employed and the results that may be expected to follow careful treatment:

CASE I.—Mr. M., aged 34 years. Extensive sycosis covering the entire back of the neck and extending up two inches above the hair margin. Treated for one year by epilation, applications of anti-

septic ointment, etc. X-rayed 24 times, with complete epilation of whole of diseased area. Some recurrence after two months, which responded promptly to treatment. No recurrence has appeared in two years. The improvement did not appear until a considerable reaction had developed, and epilation was delayed until the fifteenth treatment.

CASE II.—Mr. McM., aged 40 years. Severe form of sycosis, involving the entire upper lip, of two years' standing. Some small areas had been cured by the application of silver nitrate stick, with scarring as a result. This case responded nicely to a low x-ray tube, and epilation was prompt, appearing at the ninth treatment. The result was very good, and there is no recurrence after two years.

CASE III.—Mr. J., aged 60 years. Sycosis of the face, the entire left side of the beard being a mass of crusts. Epilation and antiseptic dressings had done some good a year previously, but he objected to the pain of the epilation forceps. This case required three series of treatments before the disease was eradicated. Several times apparent cures were obtained, but a fresh outbreak would occur.

Sycoses, like lupus, must be treated for some time after all trace of infection has vanished, or reinfection will be prompt.

Jamieson ¹ reports 30 cases of favus, 12 of sycosis, and 2 of mycosis fungoides treated by the x-rays. The sycosis cases were intractable. The result of treatment was disappearance of the pustules and a transitory depilation. Relapses were frequent, except where the disease was thoroughly eradicated. His results in favus were favorable, and were obtained without much reaction. One of the patients with mycosis fungoides has remained well for 18 months.

Gamlen ² reports a case of sycosis involving the beard, eyebrows, and eyelashes. Sixteen applications of ten minutes' duration each from a low tube completely removed the scabs and hair. There was no return of the disease in 8 months. Rhinehart ³ reports a case of sycosis treated successfully, as does Scholtz.⁴ Pusey ⁵ reports a

¹ Medical Press, Jan. 13, 1904.

² Archives of the Röntgen Ray, Sept., 1904.

³ Philadelphia Medical Journal, 1902.

⁴ Archives for Dermatology and Syphilis, 1902.

⁵ Röntgen Rays in Therapeutics and Diagnosis, 1904.

successful case of non-parasitic sycosis, with photographs, before and after exposure to the x-ray. The case was one of moderate severity and extent, but typical, and had resisted eight months' treatment locally. In four months a perfect and permanent cure resulted.

Acne.—Some of the most brilliant results accredited to radiotherapy have been achieved in the treatment of this peculiarly resistant affection. *Acne vulgaris* seems to be particularly amenable to radiation. *Acne rosacea*, while more resistant, yields in time to proper treatment. There is no class of skin disease in which the results following proper treatment are more certain, more exact, perfect, and satisfactory. It can be stated, with the assent of the large majority of experienced therapists, that every case of pustular acne may be permanently and completely cured with an excellent cosmetic effect.

If the treatment be long drawn out and a pronounced reaction avoided, the disappearance of pustules and the subsidence of the inflammation will occur, but the resulting effect is marred, inasmuch as atrophic change will have taken place in the skin, resulting in a smooth, shiny surface, covered here and there with a multitude of finely drawn wrinkles.

The following cases outline the method of treatment which I have found most efficient in this disease:

CASE IV.—Mrs. W. A chronic case of most aggravated pustular acne in a woman of 22 years, which had resisted every form of treatment save x-ray. Her face looked like that of a case of confluent smallpox. She wore at all times a double veil, and even the eyebrows were the seat of numerous large pustules. The skin was full of abscesses, which, when lanced, would evacuate often as much as 10 drops of pus. She received 10 treatments with a low tube, of 15 minutes' duration each, at a distance of 8 inches, and a decided reaction was produced. Following this there was a remarkable change in the skin. Many of the abscesses discharged, the pustules dried up, crusted, and scaled. The face became deeply pigmented, and the skin felt drawn and tense. A new crop of pustules promptly developed, and treatment was resumed, but exposures of 10 minutes were now given. At the end of the twenty-fifth exposure she was discharged without a single papule or pustule, and has not shown one in a year. This case alone would commit me for all time to the treatment of acne by x-rays.

CASE V.—Mr. B., aged 20 years, a student. Profuse crop of acne pustules covering face and neck. Treated 26 times, with disappearance of all acne, and also of a troublesome seborrhea of the nose. There is no recurrence in one year.

CASE VI.—Mr. M., a student, aged 18 years. A similar case of acne, treated at the same time as Case V. He received 20 treatments, with a very good result, but returned a year later in the same condition as at first. Under proper attention to elimination and a few more exposures he recovered promptly (Fig. 9).

CASE VII.—Mr. M., aged 16 years, a student, brother of patient VI. He came with his brother each day and received the same treatment; recovered and relapsed at the same time, and under the same treatment again recovered.

CASE VIII.—Miss L., aged 20 years. Pustular acne confined to the forehead and cheeks. Treated three weeks, and then allowed to omit treatment for one month, when six exposures were made. In spite of a very delicate skin, the resulting cosmetic effect was all that could be wished.

No matter how complete and satisfactory the result may appear, recurrence is apt to follow in those patients who suffer a considerable degree of colotoxemia. The skin, if called upon to perform vicarious elimination, is apt again to suffer, and a new crop of acne is the result. This has been my experience in a number of cases. A little more radiation and some attention to elimination will be followed by a permanent cure.

In this disease I prefer to produce, as quickly as possible, a mild degree of dermatitis. The desired stage is usually reached by the tenth treatment, three weeks having elapsed from beginning the treatment. The patient is then allowed to discontinue treatment for two weeks, an emollient being meanwhile applied; after the interval of two weeks the acne is usually found to be much benefited, the dermatitis having subsided and a majority of the pustules having disappeared. Treatment is resumed actively for three weeks every other day, and then discontinued for a period of two weeks, elimination meantime being carefully supervised. At the end of this time a third series of treatments is rarely necessary. The lowest possible tube, strongly excited and at a distance of 10 inches, is employed, and the hair and eyes carefully protected. In some patients the mucous membrane of the lips requires protection, in



FIG. 9.—Severe case of pustular acne. (On account of the nature of the lesions, the condition is ill adapted for photographic reproduction.)

others this membrane seems quite tolerant and participates but little in the reaction.

Acne rosacea and seborrhea are a little more resistant, but equally good results are obtainable by the exercise of patience and employment of the foregoing technic.

Zeisler⁶ reports 34 cases of acne, of all degrees of severity, treated with very good results. His technic consists in the employment of the soft tube at a distance of 20 to 40 centimeters, with three treatments a week for a period of two or three weeks. This is then decreased to two treatments, and later to one, a week. He observes the beneficial action during the second week and a permanent influence upon seborrhea oleosa, when present; some of his most severe cases have been cured in from 4 to 6 weeks. He compared his uniformly good results under radiotherapy with his former hard and persistent treatment in incising, curetting, applying of caustic, etc., and only regrets that knowledge of the therapeutic value of this agent was not prevalent years previously.

Schamberg⁷ declares the Röntgen rays to be extremely valuable in acne, in which disease the most brilliant results are obtained, even in long-standing cases.

Psoriasis.—The treatment of psoriasis by radiotherapy is attended with considerable difficulty: (1) On account of the large extent of surface involved in many cases; and (2) because of the development during radiation of other areas of disease distant from the part under treatment. The result obtained, while frequently satisfactory, often proves to be temporary and disappointing.

Schamberg⁸ claims the effects of the x-rays in psoriasis to be temporary only, and relapses as common as under other methods of treatment. On account of the large area frequently involved, treatment must be undertaken with great care, lest an extensive dermatitis occur and endanger the life of the patient.

Gamlen⁹ declares, on the other hand, that all skin manifestations of psoriasis, no matter how severe, can be entirely eradicated by x-ray treatment. The early results are not encouraging, but persistence in treatment is followed by an exfoliation of the silvery

⁶ Jour. Amer. Med. Assoc., 1903.

⁷ Amer. Medicine, Dec. 13, 1904.

⁸ Amer. Medicine, Dec. 19, 1903.

⁹ Archives of the Röntgen Ray, Sept., 1904.

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scales and the surrounding healthy epidermis; some stain indicative of the former site of the disease remains, but this usually disappears. He reports the case of a physician who had been subject to psoriasis for 19 years, the disease being for the most part confluent and almost universal. The condition was severe enough to unfit the patient for his professional duties as a physician for some months each year. The x-rays were applied for 12 consecutive days for 20 minutes with a low tube at 10 inches distance. Later the dosage was reduced. The arms showed a severe reaction, which, however, did not appear upon the anterior surface of the chest, abdomen, and thighs until a week later. The dermatitis on the arms was severe enough to cause some blistering, but upon the rest of the body a dry desquamative dermatitis resulted. Coincident with the disappearance of this, the skin became smooth; the patches of psoriasis, both old and new, were entirely gone. No recurrence had shown itself after 9 months.

In my experience, the disease is usually so extensive as to render radiation a proceeding fraught with considerable danger. When a few small areas only are involved, the treatment may be undertaken without hesitation and with a fair degree of temporary success.

Eczema.—The anodyne effect of exposure to the x-rays is of value in the treatment of eczema, and is usually manifested after a few treatments. In the few cases (all acute) that I have treated this effect has been constant and complete. At no time has it been necessary to produce even erythema in order to promote a return of the skin to a normal condition and relieve the distressing itching. Owing to the great extent of surface involved which must be exposed, great care must be exercised.

Gannett¹⁰ reports a case of fatal burn in which this caution was neglected. Successful results are reported by Müller,¹¹ Smith,¹² Zeisler,¹³ Schamberg,¹⁴ and Gamlen.¹⁵

Lupus.—Some of the most brilliant cures, aside from the work of Finsen and his followers, have been obtained by radiotherapy.

¹⁰ Amer. X-Ray Journal, March, 1904.

¹¹ Münch. med. Woch., June 7, 1904.

¹² Jour. Advanced Therapeutics, May, 1904.

¹³ Jour. Amer. Med. Assoc., 1903.

¹⁴ Archives of the Röntgen Ray, No. 47, p. 33.

¹⁵ Ibid., No. 50, p. 73.

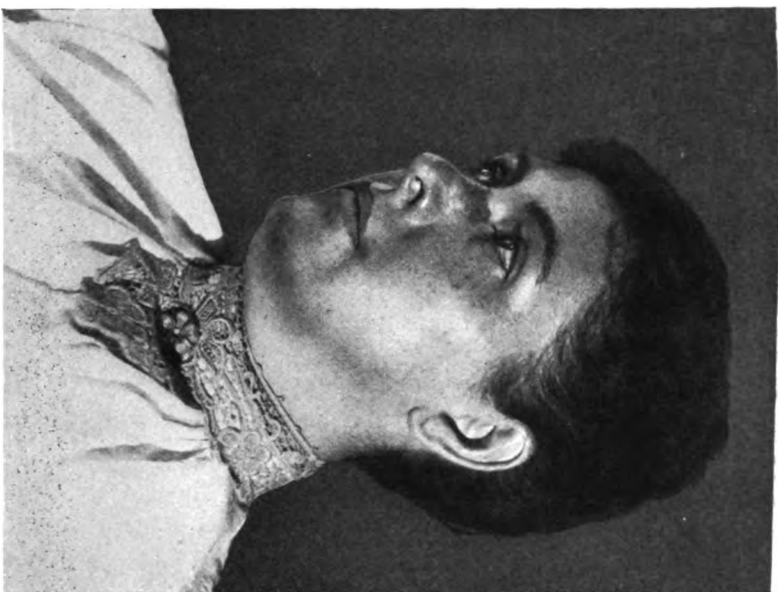


Fig. 10.—Lupus erythematosus before treatment.



Fig. 11.—Lupus erythematosus after 8 months' treatment with the x-rays. No recurrence in two years. (Same patient as in Fig. 10.)



FIG. 12.—Lupus vulgaris before treatment.

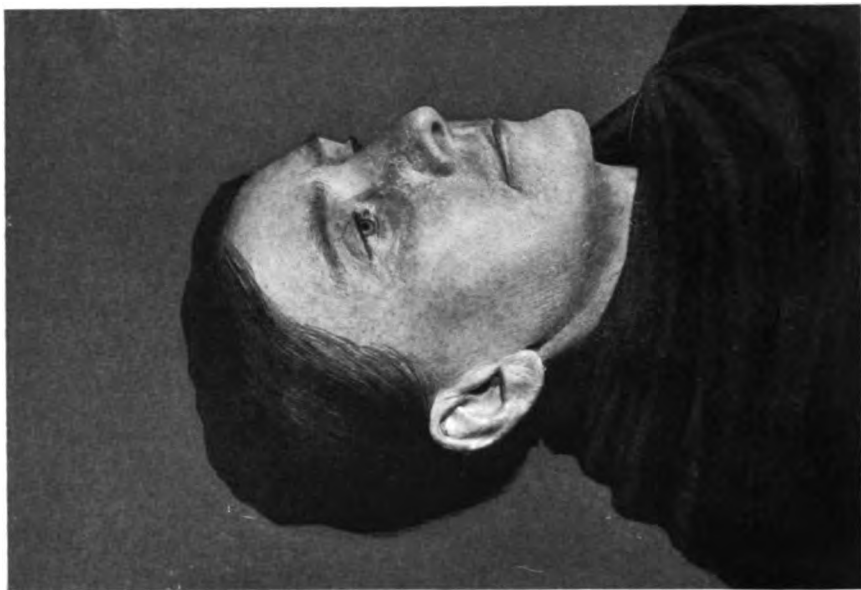


FIG. 13.—Lupus vulgaris after 8 months' treatment with the x-rays.
(Same patient as in Fig. 12.)

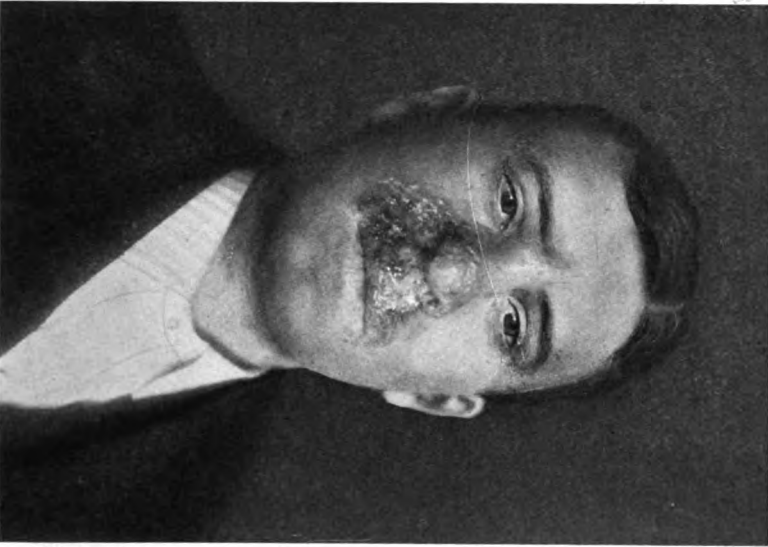


FIG. 14.—Lupus vulgaris after 2 years' treatment with caustics, curettement, etc.



FIG. 15.—Lupus vulgaris 2 years after 8 months' treatment with the x-rays (Same patient as in Fig. 14.)



FIG. 16.—Lupus vulgaris undergoing malignant transformation. The present condition followed several years' treatment by caustics, tuberculin injections, etc.



FIG. 17.—Lupus vulgaris after 3 months' treatment by the x-rays. (Same patient as in Fig. 16.)

Some of the late work reported has been done by Pernit,¹⁶ Williams,¹⁷ Gottheil,¹⁸ Campbell,¹⁹ Morton,²⁰ Edwards,²¹ Pfahler,²² Smith,²³ Schiff,²⁴ Jacob,²⁵ Hall Edwards,²⁶ Schamberg,²⁷ Jamieson,²⁸ Pusey,²⁹ and Bulkley.³⁰

I have treated 20 cases of lupus, 12 of lupus vulgaris, 5 of lupus erythematosus, 1 of lupus hypertrophicus cum sycosis, and 1 of lupus exedens. Of the 12 cases of lupus vulgaris, 10 are permanently cured, 1 discontinued treatment, and 1 has undergone an epitheliomatous change. This patient did well for two months, then the process became more active, and radiation seemed powerless to influence it. The process at present seems to be becoming less active and more chronic, and radiation will be resumed. Of the cases of lupus erythematosus, 4 are cured, 1 discontinued treatment, and 1 was abandoned after several months had demonstrated that x-ray and Finsen light were powerless to effect cure in my hands. In my early work it was my practice to proceed slowly, avoiding a reaction, but the prompt appearance of recurrence after two or three months apparent cure has led to a decided modification of my technic. I now am in the habit of attacking these cases vigorously and suspending treatment only upon the appearance of a decided degree of dermatitis. This is allowed to subside completely, whereupon a second series of exposures are begun, and continued until a mild dermatitis is again produced. Under this procedure I have had no trouble from recurrence. Except in those cases in which caustics, curettement, etc., have previously destroyed tissue, the cosmetic results are usually excellent (Figs. 10 to 17).

¹⁶ Lancet, Sept. 6, 1902.

¹⁷ Virginia Medical Semi-monthly, Nov. 13, 1903.

¹⁸ International Journal of Surgery, Oct., 1903.

¹⁹ Ibid.

²⁰ Medical Record, July 25, 1903.

²¹ Amer. X-ray Journal, Oct., 1903.

²² Archives of the Röntgen Ray, July, p. 258.

²³ Advanced Therapeutics, May, 1904.

²⁴ American Electro-therapeutic and X-ray Era, p. 325, Sept., 1903.

²⁵ Archives of Electrology and Radiology, March, 1904, p. 102.

²⁶ Archives of the Röntgen Ray, No. 48.

²⁷ Ibid., No. 47, p. 33.

²⁸ Ibid., No. 43, p. 152, 133 cases.

²⁹ Röntgen Ray in Therapeutics and Diagnosis, 5 cases.

³⁰ Amer. Medicine, Nov. 19, 1904.

Scrofuloderma and Tuberculous Adenitis.—I have treated 10 tuberculous ulcers, with good results in most cases (Figs. 18 to 21),—save that these patients are always prone to develop other ulcers in parts remote from those originally treated. In one case, instead of the usual subsidence of the low-grade inflammation characterizing these ulcers, the surrounding tissues simply broke down and resulted in a marked enlargement of the original ulceration. This patient had had repeated operations upon similar ulcers which attempted to heal, then broke down again. In tuberculous adenitis the results have been good, except when treatment was pushed too rapidly, resulting in a breaking down of the glands and formation of abscesses, thus delaying the convalescence. When treatment is properly administered and care is taken to avoid rapid destruction of the glandular masses, they undergo fibroid degeneration, and finally can be discoverable only upon careful palpation as small, intensely hard tumors.

These cases require a technic similar to that described in full presently under carcinoma of the breast, inasmuch as it is necessary to influence the whole of the tumor mass, and not simply the skin overlying the enlarged glands.

Nævi.—The treatment of hairy and pigmented nævi, unless of large extent, is best attempted by careful electrolysis. In my experience the treatment of these growths by radiation is tedious, and scarring may result. Vascular nævi are easily and successfully treated, and results have been quite satisfactory when a sufficient reaction to destroy the small vessels was produced early and maintained for a sufficient time.

Pfahler³¹ reports 2 cases of nævi, one of great extent, successfully treated by the x-rays. Dunn³² reports a case of a large angioma treated by the x-rays, with a disappearance of the coloration and a return of the skin to normal, save that the treated area had a shiny glazed appearance.

Keloid.—Success in the treatment of keloid has been attained by Pusey,³³ Pancoast,³⁴ Harris,³⁵ Gamlen,³⁶ and many others. Keloid

³¹ Archives of Electrolgy and Radiology, July, 1904.

³² International Journal of Surgery, 1903.

³³ Röntgen Rays in Medicine and Diagnosis.

³⁴ Amer. Röntgen Ray Society, 1903.

³⁵ Archives of the Röntgen Ray, p. 30, No. 47.

³⁶ Ibid., No. 50, p. 76.



FIG. 18.—Scrofuloderma.



FIG. 19.—Scrofuloderma before treatment.



FIG. 20.—Scrofuloderma after 3 months' x-ray treatment. (Same patient as in Fig. 19.)



FIG. 21.—Tubercular ulcer. Healed by 15 x-ray treatments.

usually requires prolonged and heavy radiation, and the tendency to recurrence is marked. The cosmetic result is usually good.

RADIOTHERAPY IN MALIGNANT DISEASE

The treatment of the various forms of malignant disease by radiotherapy has been so thoroughly investigated by a host of observers that it has been accorded a full degree of recognition by the profession. Early enthusiasm and optimism, which commonly attend the advent of any new therapeutic measure, have given way to quiet acceptance of the demonstrated value of the agent and a determination to define its limitations and contraindications.

It is in the various forms of superficial epithelioma that the most spectacular work has been accomplished, but since these cases were not necessarily hopeless, its greatest value undoubtedly lies in its power to influence the more malignant and hopeless growths, carcinoma and sarcoma. The percentage of success attending the treatment of primary epithelioma is, and should be, very high, and as experience begets a more perfect technic this percentage will no doubt increase. The failures and partial successes will be found among such cases as are seen in the large charitable institutions; old, feeble, ill-nourished men and women, worn out with the privations and excesses of life. Patients with Bright's disease and diabetes, chronic syphilis, poor reparative action of the tissues, lowered metabolism, incompetent excretion, etc., and with no power of resistance against the inroads of malignancy, are unfavorable subjects. They are an easy prey to any disease, and especially do they fail to resist the attacks of malignancy. Frequently, when submitted to radiotherapy, the area of apparently healthy tissue surrounding the growth, which, as well as the lesion itself, must always be rayed, will simply break down equally with the epitheliomatous tissue, make a few abortive and feeble attempts at repair, and then participate in the epitheliomatous degeneration. In many cases patches of chronic irritation of the cutis may be observed in many parts of the body, which require only a slight over-stimulus to join the malignant process. When the disease is primary, the prognosis is usually much better than in those cases of epitheliomatous degeneration following upon a preëxisting skin lesion, such as lupus or eczema.

In every case of malignant disease the operator must constantly

strive for two aims: (1) To keep elimination up to the normal, and (2) to limit and prevent metastasis. He must treat the patient, not the growth. Elimination must be maintained or treatment discontinued. Failure to observe this caution will result in toxemia or rapid increase in the size and activity of the growth, and probably metastasis.

Technic.—In the event of an epithelioma involving the nose, for example, the surgical treatment of which would result in the loss of a considerable portion of the organ, with great resulting disfigurement, the patient is suitable for radiotherapy, and the results usually obtained are all that can be desired (Figs. 22 and 23). On account of the location metastasis is unlikely, and the only precaution that must be observed is to proceed so as to save as much of the nose as possible. The urine having been examined and found in fair condition, and the patient warned of the necessity of free activity of the bowels and skin, the operator is ready to proceed to treat the lesion. A mask of lead foil, such as shown in Fig. 7, is made and applied to the patient, care being taken to have the opening of sufficient size to expose all of the growth and a liberal margin of apparently healthy tissue around it.

Protection for the patient being assured, protection of the operator must be attended to. The physician who intends to do much work and still preserve his health and comfort will do well to follow these directions closely: Have built two or three screens, such as are shown in Fig. 8, covered with sheet lead weighing at least $2\frac{1}{2}$ pounds per square foot. One of these screens should at all times stand between the operator and the tube. The use of tube covers, such as the Freidlander shield (Fig. 5), is a protection to the operator as well as to the patient, but even if these are used the screen illustrated should not be dispensed with. Of course, if a single exposure is to be made at intervals of a day or two, the operator will not suffer, but if he remains, as I have, constantly for hours every day in the x-ray room, he will as surely suffer, as have almost all the older men doing this work.

Tube Distance.—In the treatment of epithelioma the tube should be placed at a distance of 8 inches from the surface of the growth and a current of 1.5 milliamperes passed for 10 minutes. The vacuum of the tube should be quite low. Penetration is neither necessary nor desirable, and a tube that will just outline the bones of



FIG. 22.—Epithelioma of the nose (recurrent) before radiation. Mr. K., aged 77 years. Location, right side of nose, entire ala destroyed. Duration, eight years. Began as a small pimple, which remained quiet for several years, then spread. Previous treatments, arsenic paste, curettement, etc. Mother died of cancer of the lower lip. Number of treatments, 22. Result perfect (see Fig. 23). No recurrence in two years.



FIG. 23.—Epithelioma of the nose. Result obtained after 3 months' treatment with the x-rays. (Same patient as in Fig. 22.)



FIG. 24.—Type of superficial epithelioma, amenable to x-ray treatment. Cured in 3 months.

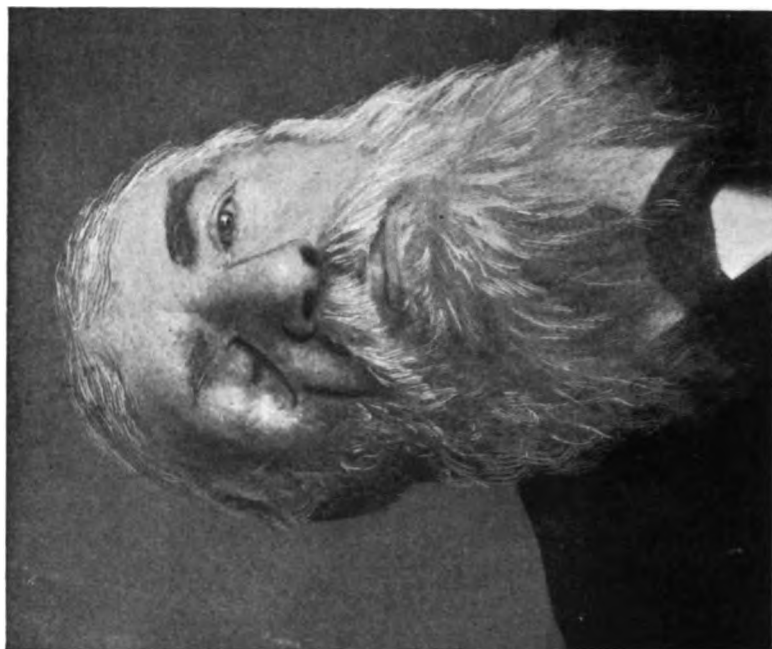


FIG. 25.—Epithelioma of the right orbit, destroying the fundus and lids. Rev. D., aged 70 years. Treated four months, and the result as shown is like an enucleation. Freedom from recurrence for one year, when a slight ulceration began in the center of the orbital cavity, which would heal under treatment, then promptly break down again, and inclement weather preventing his attendance, the disease progressed rapidly to a fatal termination.



Fig. 26.—Epithelioma of the lower jaw. Mr. L., aged 50 years. Duration, nine years. Began as a small ulcer on the lower lip. Previous treatment, arsenic paste; curettement. General condition bad. Entire mouth involved. Chin is a honeycombed purulent mass. Treated three months. Much benefited. Ulceration healed. Discharge from sinuses in chin ceased. Able to masticate food. Went home and disease remained inactive for a year, then became active and death followed in two years.

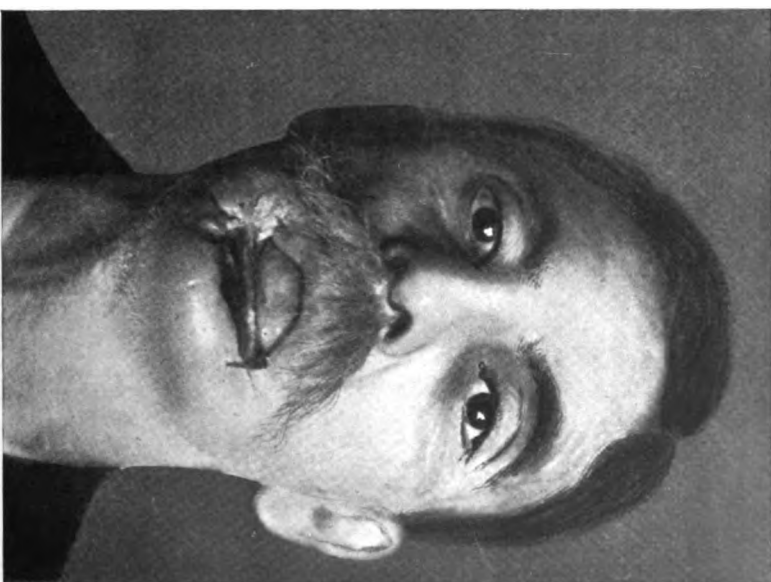


Fig. 27.—Result obtained by x-ray treatment of patient shown in Fig. 26.

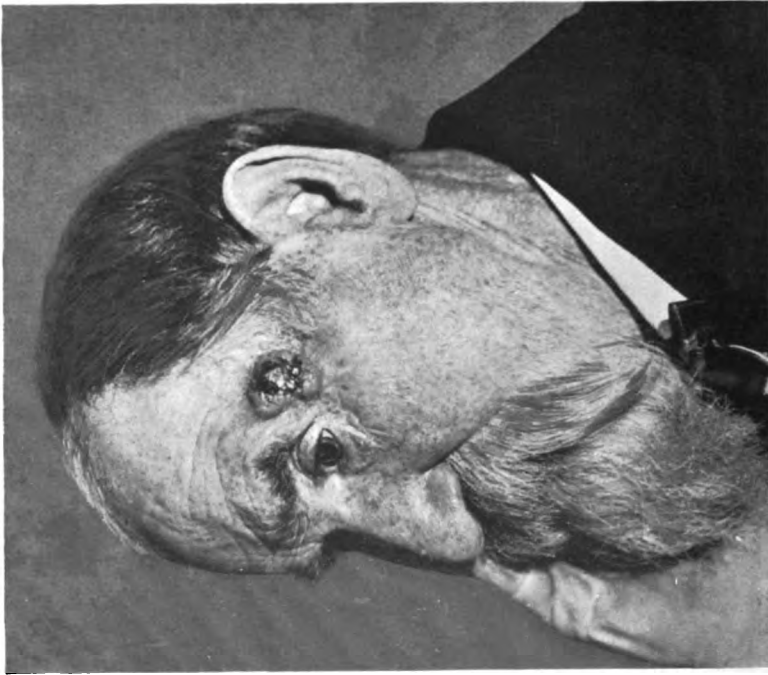


FIG. 28.—Epithelioma of the temple and lower lip. Mr. McC., aged 73 years. Began as a small fungating growth in the center of the lower lip. Treated by cautery and extensive resection of the lip. Recurrence prompt. Entire mucous border of lower lip is an open excavated ulcer with sharp edges and bathed in foul pus. Submaxillary glands are swollen and tender. On the left temple is a raised fungoid mass an inch in diameter. Lip treated 25 times and healed kindly. Temple given 8 treatments and second degree burn produced, followed by disappearance of the mass.

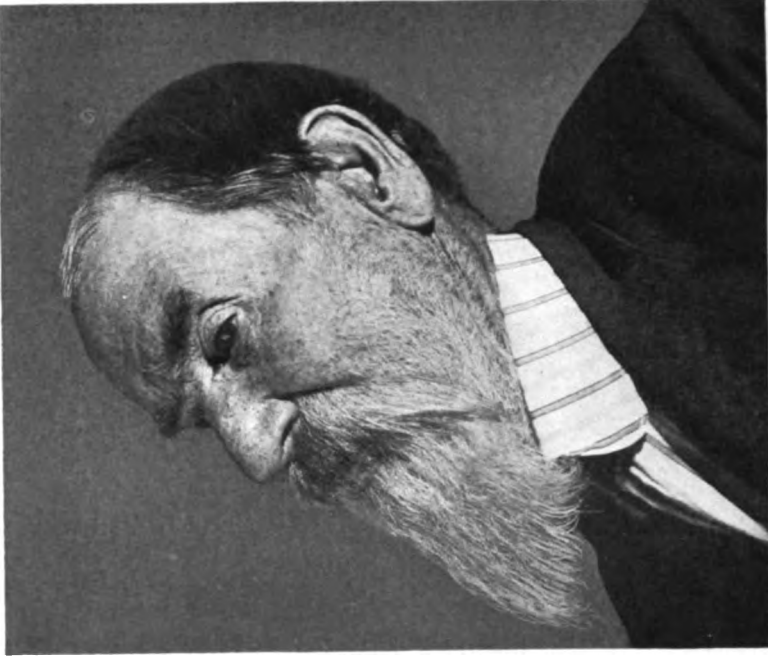


FIG. 29.—Patient shown in Fig. 28 after treatment.

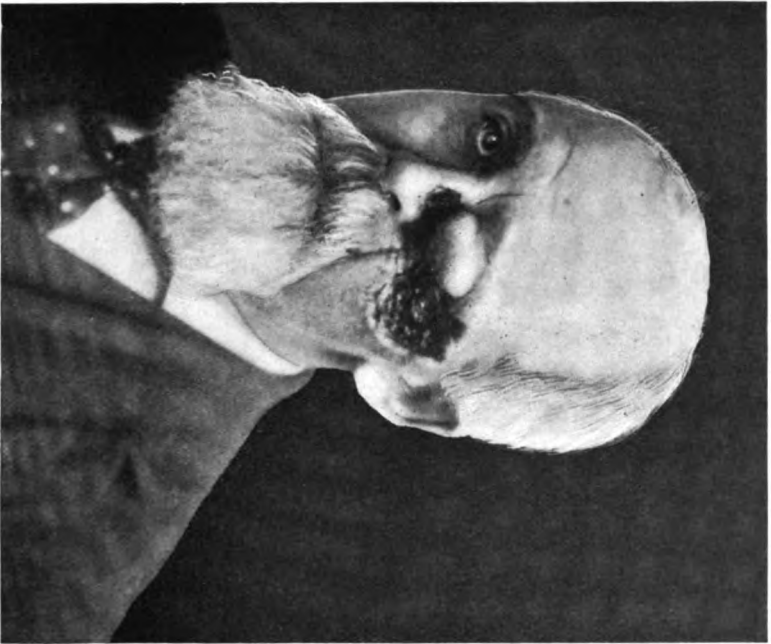


FIG. 30.—Epithelioma of the orbit and face. Mr. S., aged 65 years. Duration, 15 years. Began as a small ulcer on the nose and spread slowly. Entire side of face and nose is an open sore, discharging profusely and very foul. Eye destroyed. Upper lid swollen and hard. Previous treatment, arsenic paste. Treated for one year. Marked improvement. Ulceration healed but eyelid remained enlarged. Ulceration remained closed until his death from heart disease 3 years later.

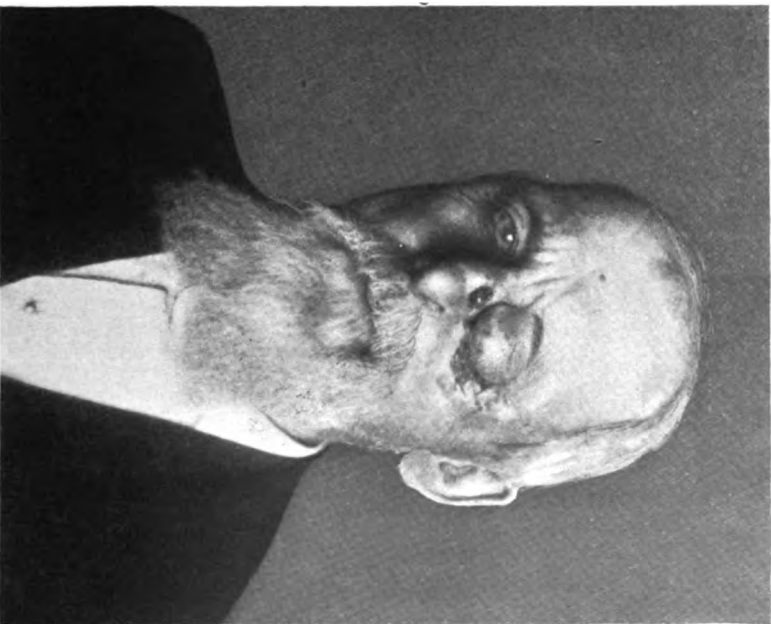


FIG. 31.—Result of x-ray treatment of patient shown in Fig. 30.



FIG. 32.—Epithelioma of the angle of the mouth. Miss I., aged 10 years. Duration, 7 years. Previous treatment, caustics. Ulceration an inch long and a half inch wide, discharging yellow seropus. Treated 26 times. Result perfect. No recurrence in one year.



FIG. 33.—Result of x-ray treatment of patient shown in Fig. 32.

the fingers is high enough. In this condition I use habitually a tube so low that it requires the insertion of considerable spark-gap to induce it to give off x-rays at all, but I do not advise the use of such an active tube in the hands of a novice.

The above procedure is repeated on the following day and on each day until the tenth. By this time there has usually appeared a considerable degree of warmth in the surrounding test area of skin, and the discharge (if present) from the ulceration is markedly increased. Treatments are now reduced to three a week, and if the reaction seems to be severe, the time of exposure is cut to 5 minutes, or treatment is omitted for a few days and antiseptic washes applied. If the tongue is clean, the bowels open, and the urine normal, treatment is begun as soon as the reaction subsides, and is continued at intervals of every other day for two or three weeks. By the end of this time the discharge has ceased and granulation is usually going on rapidly. Care must be taken not to destroy these healthy granulations by over-radiation. A few treatments should now be given without the screen or mask, so as to affect any possible foci of disease in the vicinity of the growth, and the patient then allowed to stop treatment for two weeks. At the end of this time, if the growth has disappeared and is replaced by healthy connective tissue, the patient may be discharged, with instructions to return for an inspection of the scar, in one month; on his return, if the slightest symptom of recurrence be present, treatment should be resumed as before.

If these slow-growing epitheliomas be x-rayed for long periods with a high tube without producing much reaction, they will slowly heal, but often the edge, instead of melting down (as is the case under more vigorous measures), will become elevated, indurated, covered with newly-formed blood-vessels, and shortly a carcinomatous change will appear in the edge, rapidly growing and exceedingly refractory to radiation. I have observed this in my own practice and in that of others, but it is not as common as it was when the high tube, actuated by a static current, was a favorite among certain physicians.

Recurrence.—If the patient be of middle age and in fair physical condition, the results obtained will usually be permanent, but if the contrary, a careful watch must be kept for recurrence. In my experience, these patients are prone to relapses during the third year following an apparent cure.

The mistake most commonly made in treating epithelioma by this method is that of continuing radiation, day after day, in small doses, without any definite point in view, but vaguely expecting the ray to cure the disease. X-radiation has no more power of independent action than has arsenic: a certain dose at certain intervals may be employed to cure a certain disease, but it is given for the production of certain definite physiologic activity. When this has been obtained, the dose is continued if this effect is to be maintained; if not, the administration of the remedy is stopped. So with radiation. Certain definite tissue changes occur coincident with and subsequent to the administration of a therapeutic, not a toxic, dose, and the dosage must be as carefully adjusted to the result as would any other toxic active therapeutic measure.

In radiotherapy, when in doubt, stop radiation. Wait until you see the ultimate result of the cumulative dose already administered. The sooner the profession realizes that the possession of a more or less costly, spectacular, and inefficient collection of x-ray apparatus does not argue its possessor a competent radiotherapist, any more than the purchase of a few instruments makes one a safe abdominal surgeon, the better for the profession and the public. It is at this point that the inexperienced radiotherapist does harm to his patient and himself, but by simply stopping all treatment for a few days he can determine just how much actual good his work has done, and by the behavior of the lesion judge whether it is wise to continue to break down tissue or to allow the lymphatics time to carry off the results of his radiation and clean up for another series of treatments. It is poor practice to continue to x-ray a rapidly diminishing and granulating epithelioma. It is much safer to wait until the activity occasioned by treatment has decidedly diminished, and then administer sufficient radiation to bring on active tissue change.

When the lesion under treatment is situated in a region liberally supplied with lymphatics, as, for example, those epitheliomas often seen in the center of the lower lip, the technic is decidedly changed. The question of operative interference or assistance must be squarely met. Upon the correctness of the judgment of the operator depends a human life in every such instance. It is a dangerous thing to attempt to formulate rules for such a contingency, but the following suggestions may be of value in arriving at a conclusion:



FIG. 34.—Epithelioma of the bridge of nose, an inch long, three-quarters of an inch wide. John T., aged 46 years. Duration, three years. Previous treatments, zinc chlorid. Treated with the x-rays, 20 times. (Complete disappearance. No return in three years.

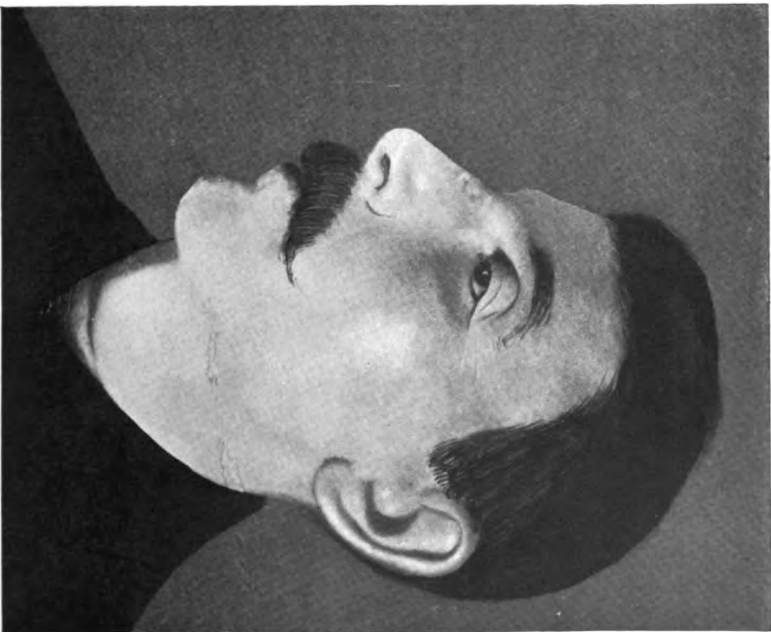


FIG. 35.—Result of x-ray treatment of patient shown in FIG. 34.



FIG. 36.—Epithelioma of the face. ; Robert M., aged 67 years. Duration, 15 years. Began as a small ulcer on the side of nose. Previous treatment, arsenic paste. Right eye blind from gunshot wound. Entire left side of face involved. Left eye has both eyelids involved. Discharge was profuse and foul, but cleared up after six treatments. Treated 3 months with complete disappearance of the growth and healing of ulceration.



FIG. 37.—Result of x-ray treatment of patient shown in Fig. 36. Face is disfigured from failure of granulation to cover more than facial bones.



FIG. 38.—Epithelioma of the left brow and temple. Mrs. R. Duration, five years. Treated 20 times; scar is soft and scarcely visible. No sign of recurrence in six months.



FIG. 39.—Result of x-ray treatment of patient shown in Fig. 38.



FIG. 40.—Epithelioma of angle of mouth and inside of upper lip. Mr. W. Treated 3 months; would not heal until second degree burn was produced. Result is good from cosmetic standpoint, and there is no recurrence after one year.



FIG. 41.—Result of x-ray treatment of patient shown in Fig. 40.



FIG. 42.—Epithelioma involving entire orbit. Mr. W., aged 65 years. Previous treatment, pastes. Treated 10 times, with great improvement. Stopped treatment because he was told Röntgen-rays would burn his eyes out.

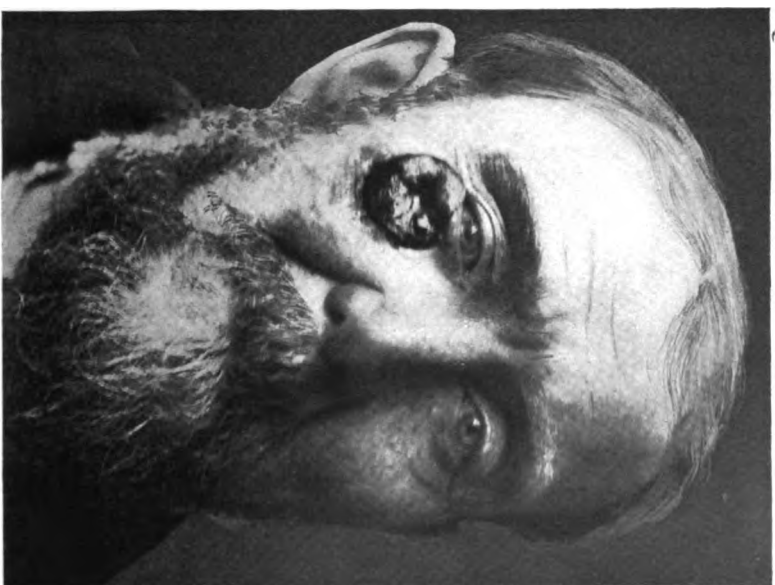


FIG. 43.—Epithelioma of lower lid following entrance of piece of steel a year previously. Mr. D., aged 50 years. Elevated bleeding rose-like mass an inch in diameter, with depressed center and piled up edges. Treated 10 times in 6 weeks. Complete recovery, with very little ectropion and no return in 3 years.



FIG. 44.—Epithelioma of the nose. Mrs. G. G., aged 67 years. Location, entire nose. Began as belf on the nose, following amallipox, 30 years ago. The belf left a wart, which remained quiescent for 20 years, then began to grow until the present condition was reached,—cauliflower nose with a large sinus leading into the left naris. Treated 2 months. Number of treatment, 30. Result perfect. No recurrence in 2 years.



FIG. 45.—Epithelioma of nose. Mrs. H. Fungating mass $\frac{1}{2}$ x $\frac{3}{4}$ inch on the end of the nose. Cured in 10 treatment. No recurrence in 2 years.

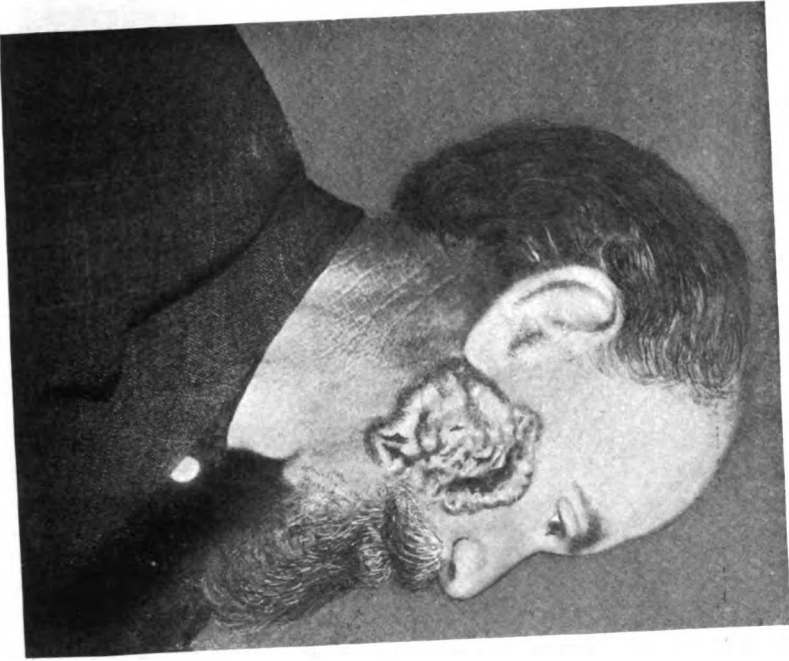


FIG. 46.—Epithelioma of cheek before treatment. Mr. H. Durnton, 15 years. Remained slow and quiet up till 6 months ago, when a fall, striking the growth on some timber, caused it to spread rapidly and pain greatly. Treated one month and became a simple ulcer, which healed without further treatment.



FIG. 47.—Result of x-ray treatment of patient shown in FIG. 46, when treatment was discontinued.

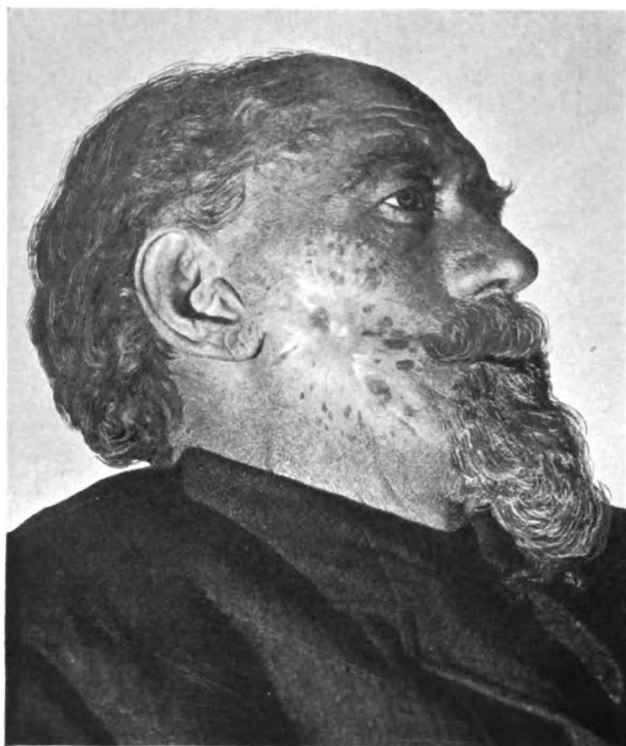


FIG. 48.—Result of x-ray treatment of patient shown in Figs. 46 and 47, 3 years after x-ray treatment was discontinued.

- (1) Is the lesion deeply seated?
- (2) Are the submaxillary glands enlarged and swollen?
- (3) Is the physical condition of the patient such as to justify an operation?
- (4) Can the lesion be completely removed surgically?

If these questions can be answered affirmatively and the patient's consent obtained, the best thing to do is to x-ray the enlarged glands and the entire lip and chin energetically every day for six days with a tube placed at a distance of 10 inches from the surface that will just penetrate the arm, then do a radical operation, and on the fifteenth day after operation commence prophylactic x-*raying*.

If the lesion be superficial, with no submaxillary or other glandular involvement, and the patient's condition be good, the growth may be attacked by means of the x-ray alone,—with good results in many cases (Fig. 24). In two such patients, who presented no signs of metastasis and whose general physical condition was good, I have accomplished a speedy and permanent cure. In another patient, who presented such involvement of the entire lower lip as to preclude attempts at removal short of a resection of the entire lip and a plastic replacement, radiation for a few weeks circumscribed the growth to a small area in the center of the lip, which was then removed, with good results. The tendency to general metastasis in cases of malignant disease in this particular location is very great, and if screens are employed and the x-*raying* of the glands of the neck be neglected, metastasis will almost certainly appear.

Epitheliomas about the eyelids are best treated by x-rays alone, on account of the excellent cosmetic result usually obtained. Those involving the orbit almost always recur, following apparent cure by radiation, and the recurrence when again treated is very difficult to influence. Fig. 25 shows the result obtained in such a case, but recurrence a year later seemed to be uninfluenced by even heroic doses.

The accompanying photographs (Figs. 22 to 48) have been selected with a view to illustrate the results of x-ray treatment in epithelioma.

CARCINOMA

The treatment of carcinoma in its many forms and locations is the most important subject that can claim the attention of the radiotherapist. The results of surgical removal in this disease are

often good; on the other hand, operation seems oftentimes to awaken a latent malignancy which overwhelms the patient. The results of radiotherapy alone are often very good, often only temporary and unavailing.

Every patient with carcinoma should be examined by a careful, judicious surgeon who is fully aware of the limitations of surgery, as well as the immediate benefits derived by operation, and by an experienced radiotherapist who is fully aware of the exact limitation of his art. Two such men working in full sympathy and having at heart the welfare of the patient can do wonderful work. It is by the intelligent and hearty coöperation of surgery and radiotherapy that the best results in this class of cases will be obtained.

To my mind, the most important thing in the treatment of carcinoma by x-rays is the fact that certain cases are unsuitable for radiation at all, except under very rare circumstances. Carcinoma, when attacking the uterus, lower jaw, lower lip, or testicle, should be treated by as immediate and radical surgical extirpation as possible. I do not believe that this admits of any denial or argument. Every day counts, and a week may mean metastasis beyond human power of control.

Carcinoma in other parts of the body may be treated for a time by radiation, before submitting to removal, with very good results, but in the locations named the surgeon must be the first resort.

The treatment of carcinoma by radiotherapy varies with the location more than with the particular variety of growth present. Carcinoma of the face is one of the most frequent diseases one may expect to meet in radiotherapy. As a general rule, if the bone be not involved or denuded, the prognosis in early cases is fair.

In carcinoma involving the orbit, those attached firmly to the malar bone, and those in the lower lip, with submaxillary and sublingual involvement, the prognosis is not good. Carcinoma about the face usually requires quite vigorous treatment with an active tube. Irregular, half-hearted, doubtful, undecided radiations will often simply result in the development of a most active propagation of the carcinoma, with rapid development and metastasis. I have never seen a burn in a carcinoma of the face do harm, but I have seen a slow-growing scarcely clinically malignant carcinoma transform into a most active form under dilatory and inefficient treatment. In the treatment of all forms of carcinoma (and sarcoma) a most careful



FIG. 49.—Small carcinoma 10 days after complete removal by operation. The recurrence was treated and cured by the x-rays alone, but a severe toxemia was caused by the breaking down of the small tumor shown in the photograph.

watch must be kept for evidences of failure of elimination, and the treatment should be pushed as quickly as elimination may permit. Under powerful doses of x-rays the carcinomatous tissue melts down, often very rapidly, and a tremendous overload is thrown upon the kidneys (Fig. 49). At the first sign of reaction treatment should be stopped. If a tube of low vacuum with a resistance equal to 3 inches parallel spark in air with a current of 2.5 milliamperes has been used at a distance of 8 inches, this reaction will appear at about the twelfth treatment, and in a week will usually subside enough to allow a resumption of exposure.

Carcinoma of the larynx and pharynx must be attacked by combined internal and external exposure, and if good results are obtained the operator is to be congratulated. Carcinoma of the lower lip must be submitted to operation, if possible, the submaxillary and sublingual glands having first been given six exposures to the x-rays of 10 minutes each. Following operation as soon as possible the entire lower jaw and neck and upper chest should be x-rayed at intervals of three days for one month.

I have treated some patients who have recovered from carcinoma of the lower lip under radiation alone, but I have seen three valuable lives lost because the patient absolutely refused operation until too late to hope for any good result. By the method outlined above the greatest number of patients can be saved.

Carcinoma of the tongue is not common and may be dismissed with a few words. When the base of the tongue and the submaxillary glands are involved the case is hopeless, and operation will be followed by a prompt recurrence. Under these circumstances treatment by x-rays is justifiable, and if the carcinoma be of a scirrhus variety, life may be prolonged in comfort for years, in some cases. The tongue should be treated every other day and the neck x-rayed every other day. Under treatment, the pain on deglutition usually disappears promptly, and the tongue becomes mobile and painless. The patient is exceedingly grateful for the relief afforded, and, while the ultimate result is death, yet these cases are very satisfactory.

Carcinoma of the breast is the most common form of malignant disease that many men are called upon to treat. The attacks made upon those who dare to suggest anything aside from complete extirpation for the relief and cure of this disease have been very bitter.

In many cases they have been justified. Coming from the surgeon, they would be a little better received were the results of extirpation more hopeful. The brutal truth, which is the only thing worth while in this world, is this: Operation alone for the cure of carcinoma of the breast, accompanied by involvement of the axillary or the subclavicular glands, is not a success in the great majority of cases. Those men who are able to keep intelligent records of their patients and follow them for two to three years know this, and some have even dared to say it.

In competent hands radiotherapy has accomplished as favorable results in these cases, but the combination of radical operation, preceded and followed by skilful radiation, will cure a much greater proportion of patients than either method alone. In those patients who have not had the benefit of radiotherapy following removal of the breast for carcinoma, and in whom the disease has returned, a great deal can be done. The recurrence, if local, can always be cured; if, however, the other breast is involved, or the subclavicular glands on the opposite side enlarged, a general metastasis is in progress, and a stay of proceedings only need be expected. In several such cases I have succeeded in obtaining a disappearance of all outward signs of disease and a great gain in the general health of the patient lasting for several years, with no signs as yet of much loss of ground.

In the treatment of all tumors of the breast by the x-rays the tube must be placed at least 12 inches from the surface, in order that the effect on the surface may not be much greater or earlier in appearance than that occurring in the deepest portion of the growth. The time of exposure must be increased proportionately with the distance (see page 6).

It is rarely desirable or necessary to burn the skin. Such an occurrence simply interrupts treatment for a time. I have produced a permanent (two years) disappearance of large tumors of the breast in three patients without this occurring save to a very limited degree. The treatment of breast carcinomas takes time. Six months is little enough to undertake to treat such a case. In the hopeless, pitiable cases of the breast, or, better, chest carcinoma, when nothing seems worth doing, a great deal can often be done. The operator who is looking for cures to report need not bother with these, but the man with a proper conception of the duties of a physician will give these patients the best he has. The extent of the growth is such that

careless radiation simply means the early painless death of the patient by toxemia. If the patient is also able to stand operation, one or both breasts may be removed, the axillary glands having first been given 10 strong radiations. The operator must be induced to do a simple amputation with as little shock and as small a loss of blood as possible. The idea of reaching all foci of disease and removing them must be abandoned. On the fifteenth day following operation radiation should be begun, and a tube without a shield used. The entire neck and chest, front and back, and the axilla should be rayed every other day until a marked reaction occurs, and then resumed as soon as this subsides. Under this treatment pain disappears, appetite returns, and several years of useful life are often obtained.

The use of screens in the treatment of breast tumors is to be deplored. The neck, axilla, and mediastinum, as well as the breast, must be rayed if metastasis is to be prevented. The conservative, reasonable radiotherapist will receive his breast cases directly from the hands of the most able and experienced surgeons; the enthusiast will receive from these men a full measure of merited censure and contempt.

I have treated no cases of carcinoma of the stomach or bowels that had not received or been refused the benefits of surgery. In such a case, bearing in mind that all broken-down tissue must be absorbed, and hence proceeding slowly, good results may often be obtained. In cases in which exploratory incision is lacking, doubt may be cast upon the diagnosis—in the event of cure. The following is an illustrative case:

CASE IX.—Mrs. W., aged 72 years. Four healthy children. No previous serious illness. Indigestion for years. Complained for two years of burning pain in the stomach, worse after eating. Progressive loss of strength; pain slowly increased, becoming unbearable; vomiting of quantities of undigested food, with some coffee-ground material, occasionally blood. Emaciation, dysphagia, agonizing burning pain circumscribed to an area four inches about the pyloric end of the stomach. Distinct, hard, fusiform tumor, easily palpable through the emaciated abdominal wall. Weak, sleepless, moaning constantly, vomiting everything, even water, and living for three weeks on rectal alimentation. Analysis of the gastric contents is indicative of carcinoma. Diagnosis of the attending surgeon, Dr.

E. R. Gregg, was carcinoma of the pylorus. Prognosis, death. Operation refused by Dr. Gregg, on account of the condition of the patient. Radiation was begun for the relief of pain. A 12-inch western coil, Wehnalt interrupter, 60 cycle, 54 volt current, was used. G. E. tube set at 5 inches, resistance in air. Distance, 20 inches; exposure, daily for 12 minutes. After the tenth day, exposure for 15 minutes every other day. Relief from vomiting and pain followed the ninth treatment. The patient sat up on the fifteenth day. Treatment was discontinued on the forty-second day on account of some reaction in skin, and was never resumed. After one year the patient is alive and well, with no discoverable tumor and no stomach trouble.

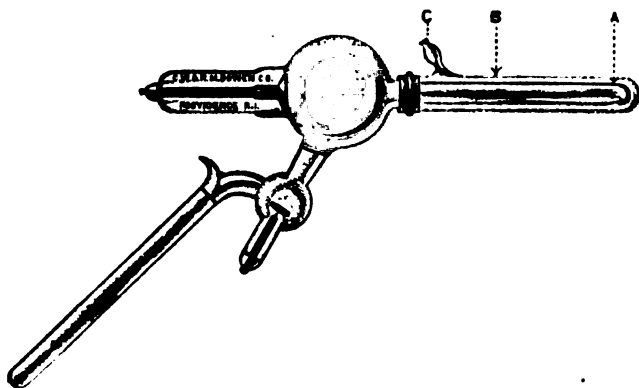


FIG. 50.—The Improved Caldwell Tube is a very desirable modification of the original designs in many cases. As shown in the cut, the tubular projection is protected by a glass outer tube, which is filled with water, while in use, thus preventing heating to the discomfort of the patient. The type is quite different from the originals. The entire tube, excepting the tip of the projection, is made of lead glass to retard the rays. It is provided with a cathode and anode located within the bulb, and so arranged as to project the rays to the point C, where they are emitted through the transparent glass composing the tip. These tubes can be made with tips of various sizes if desired.

In view of the symptoms presented, this case appears to have been one of malignant pyloric obstruction, but it yielded so readily to treatment as to justify grave doubt. The technic is that employed in all cases of abdominal carcinoma.

Carcinoma of the uterus comes within the province of radiotherapy under two conditions only: (1) When postoperative radiation is employed to prevent recurrence and free the pelvis of any small foci which may have escaped extirpation; and (2) in exten-



FIG. 51.—Melanosarcoma. Microscopic diagnosis, squamous epithelioma.



FIG. 52.—Melanosarcoma after removal by the x-rays. Recurrence in the neck 3 months later removed surgically, recurrence in one week, and death 15 days later from suffocation.



FIG. 53.—Fibrosarcoma, recurrent after 3 operative removals; cured by x-rays, and no recurrence after 3 years.

sive inoperable cases for the relief of pain and the control of hemorrhage. Postoperative x-raying should be begun as soon as the convalescence of the patient permits. The pelvic contents must be rayed from within and without on alternate days. A tube of fairly high penetration, such as would be used in the radiographing of a hip, and placed at a distance of 18 inches, is employed to ray the abdomen; for internal work, either a speculum is employed and the radiation from an ordinary tube allowed to pass through it, or the tube devised by Mr. Caldwell (Fig. 50) may be used. This tube, owing to the double thickness of glass afforded by the water-jacket, gives off but little x-rays, and the exposures must be quite long in order to obtain results. I have employed it in cases of uterine and rectal carcinoma with satisfactory results in the relief of pain and hemorrhage. All the patients treated are dead, and I have not seen anything approaching a cure in either uterine or rectal cancer.

In carcinoma of the rectum, external and internal, x-raying is usually followed by marked decrease in the size of the tumor and relief of the constipation. All external growth disappears and pain is usually greatly lessened, but the palliation in my hands, while very grateful, has been only temporary.

SARCOMA

The treatment of sarcoma by the x-rays is satisfactory or not, according to the point of view. No such percentage of successful results as attends the treatment of epithelioma or carcinoma need be expected. Sarcoma represents the acme of malignancy, and recurrence is frequently synchronous with supposed post-operative convalescence. Metastasis is widespread and occurs early. The tumor is often of enormous size, and operation is followed by severe shock. Moreover, metastasis is often seen so quickly following operation as to create a suspicion of cause and effect. Toxemia is difficult to avoid when large masses are x-rayed, and metastasis may be provoked by improper radiation. Everything seems to argue failure, and under such conditions success is rare and difficult.

Some excellent men have even doubted the possibility of success and have produced a mass of negative testimony,—series of 20 or more cases with 100 per cent. of deaths. Yet success does occur in some cases, often when unexpected, and should be all the more appreciated by reason of the rarity. I have treated many cases of sar-

coma, and can report but three cases of inoperable recurrent sarcoma successfully treated.³⁷

Cases have recurred during postoperative radiation and progressed to a fatal termination. Melanotic sarcoma in two cases has disappeared under radiation, to recur in a remote locality months after, but, in spite of all this, the possibility, even probability, of success should only stimulate the workers to a perfection of technic, which may prove successful in a fair proportion of cases. (Figs. 51, 52, and 53.)

Sarcoma is not a superficial disease, and requires entirely different treatment from most malignant growths. A tube of sufficient penetration to reach the innermost confines of the growth, placed at a distance sufficiently great to equalize the effect at the different levels, and excited strongly enough to overcome the loss by reason of this distance, solves the problem.

No screen should be used, no matter what the location. Treatment must be pushed in spite of danger from toxemia. Elimination must be forced, and strength kept up by every possible art. Failure must act as a spur to renewed endeavor. Any one may fail, and failure is not to be used as condemnatory to the means employed. No one claims x-rays as a cure for sarcoma, but when one cures a sarcoma by such means, or any other, he must be encouraged, and the result judged in accordance with the means employed. Any one could kill Goliath with a Mauser; David did it with a pebble.

Morton has reported results by the use of Coley's toxins and x-rays, and it is to be hoped he will continue his work. Hopeless cases of sarcoma may be treated for the resulting relief from pain, but if there is even a remote possibility of a cure, the case must be studied and attacked with this end in view. An x-ray burn may be produced, but this is sometimes necessary in such a case, and is certainly justified.

No man who has ever cured a case of sarcoma by any means whatsoever should allow the incredulity, ridicule, or contempt of a certain small proportion of the profession to deter him one moment from earnest endeavors to reproduce such a result.

The following cases are two of the three mentioned above, and were reported at the Fourteenth Annual Meeting of the American

³⁷ *Jour. of Advanced Therapeutics*, Nov., 1904.

Electro-Therapeutic Association, held in St. Louis, September 14, 1904:

CASE X.—Mr. W., father of a physician of Pittsburg, Pa., aged 56 years. His family history is negative. His general health was good up to four years ago, when some pain in and enlargement of the abdomen attracted his attention. The abdominal muscles, as he expressed it, seemed to be constantly cramping, and a multitude of hard globular masses in the abdominal wall became apparent. He suffered considerable pain and rapidly became cachectic. He fell off in weight, his appetite failed, and an examination of the abdomen, by his son and Dr. Adair, revealed the presence of a very extensive growth, involving the entire right rectus muscle and a large portion of the left. An operation was decided upon, and was performed by Dr. Langfitt, at the St. John's General Hospital, assisted by Dr. Adair and his son, Dr. W. The operation disclosed such extensive involvement of the peritoneum and omentum as to preclude the possibility of a complete extirpation of the growth. Dr. Langfitt satisfied himself by removing the entire right rectus, which was simply a sarcomatous mass of yellowish débris, and a portion of the left rectus, and such other portions of the growth as seemed permissible. So much of the abdominal muscle was of necessity destroyed and removed as to require the immediate application of a large abdominal binder, which the patient must continue to wear for the remainder of his days. As soon as he was able to leave his bed after the operation from which he convalesced rapidly, he was brought to me with the request that I endeavor, if possible, to inhibit the growth of such portions of the tumor as had been permitted to remain at the time of operation. He was very weak, markedly emaciated, anemic, and cachectic, and suffered considerable abdominal pain. He was discouraged and disappointed, and I did not feel that there was much to offer him. In fact, the treatment was only undertaken at the earnest request of his son and Dr. Langfitt.

Treatment was given daily for two months, with a tube of high penetration, at a distance of 18 inches, excited by a 15-inch Queen coil, vibrating interrupter, 7 amperes in the primary circuit, duration of treatment 10 minutes. The greatest care was exercised to prevent the occurrence of abdominal burns, which would have terminated the treatment, as the patient was in no physical condition to repair such a lesion. The abdomen was tanned slightly and the

pubic hair disappeared. During three months the same technic was employed, treatment being given every three days, and during the fourth month treatment was given once or twice a week. At the end of this time treatment was suspended for one month, weekly examinations of the abdomen being carefully made. The pain had disappeared during the two months, the abdominal wall had softened, and there was no evidence on palpation of the persistence of any enlarged glands within the abdomen. The patient's color was good, the appetite excellent, general health good. He had gained 30 pounds, and he remains to-day in excellent condition. The most careful and repeated examinations by a number of surgeons have failed to reveal any evidence of malignant disease.

CASE XI.—Miss O., aged 42 years, suffered from a recurrent sarcoma of the vulva. The patient in 1900 noticed a swelling and tenderness of the pubes, following a blow from the corner of a dining-room table. A swelling developed rapidly and extended into the right labium majus. The pain, which was constant, increased in severity until she was compelled to submit to examination by her family physician, Dr. Frederick, who at once recognized the nature of the trouble and advised immediate operation. The growth was removed as completely as possible by Dr. C. B. King, and an apparent cure was the result. Six months later the growth returned in the scar of the operation, and an examination of the first tumor having shown its malignant nature, a second operation was at once resorted to. This was followed by relief for several months, when the growth returned with all the old symptoms; but this time it was characterized by great rapidity in enlargement and extension, and whereas the former tumor had to a certain extent been encapsulated and discrete, this recurrence involved the skin, subcutaneous tissue, periosteum, and could not be removed surgically without damage to the urethra, labia majora and minora, and the clitoris. Under these circumstances, the surgeons decided that they had nothing further to offer, and suggested that she submit herself to a course of radiotherapy. In view of the undoubted malignancy of this growth, both clinically and microscopically, the treatment was undertaken with considerable hesitancy. A Queen self-regulating tube, set to back up a spark-gap of $3\frac{1}{2}$ inches, actuated by the discharge from a 15-inch Queen coil, vibrating interrupter, plain primary, taking 5 amperes in the primary circuit, was employed. The tube was placed at a dis-

tance of 15 inches from the lesion. Ten-minute treatments were given daily for three weeks. A lead screen, having an opening six inches in diameter opposite the lesion, was used to protect the abdomen and thighs. At the end of this time the pubic hair had disappeared, never to return. A mild degree of dermatitis was present, which caused the patient some slight inconvenience. The pain in the growth had practically disappeared, and it had ceased to enlarge. A rest of ten days was given the patient, and a dusting powder of stearate of zinc ordered. The dermatitis having subsided and being followed by a dark mahogany tan, treatment every other day, with the same technic, was undertaken for six weeks. At the end of this time the abdominal screen was discarded, a fairly high tube with good penetration, carrying a half-inch spark on the cathodal side, was employed, and treatments twice a week, at a distance of 15 inches, were given for two months. At the end of this time some vague abdominal pains which had given rise to a suspicion of pelvic metastasis having disappeared, the high tube was discarded, and a rest of two weeks given the patient. At this time there remained but two foci of disease, one the size of a lima bean, very hard and slightly movable, one-half inch to the right and one-half inch below the symphysis pubes, the other a thickening of the subcutaneous tissue, in the right labium majus. A Queen tube, sharply focussed and rich in chemical ray (a picture tube which would make a satisfactory elbow radiograph in one minute, with eight amperes and a vibrating interrupter), was now employed, placed at a distance of 10 inches from the vulva, and a first-degree x-ray dermatitis was produced. This required six treatments. The dermatitis produced the first complaint from the patient, and she was obliged to spend the most of her time at rest for a week, during which time she suffered considerable pain. This was the last treatment which she ever received, for, following recovery from this burn, every trace of the sarcomatous deposit disappeared, and there has never at any time been any indications of a return. Her general health is excellent, and she is one of those pleasing assets, a grateful patient.

GENERAL CONSIDERATIONS

In the foregoing pages an attempt has been made to treat as concisely as is consistent with clearness the treatment of the more common diseases presented for the services of the radiotherapist.

These are by no means all the conditions for the relief of which the x-rays have been tried. Good results are reported daily in such diseases as leukemia, goiter, pulmonary tuberculosis, etc., but the cases are few in number, and time must elapse before the actual value of the x-rays in these conditions is determined.

The whole subject of radiotherapy is embraced in the word technic, and this is naturally a full avowal of the personal equation. The operator at the beginning of his work is the possessor of a confused jumble of facts, fancies, and observations regarding the proper dosage of x-rays and how to judge and administer it. Experience only can correct the false and perfect the true in it all. He must proceed cautiously, knowing that every mistake will cost a success, and endeavor to perfect for himself a method of procedure founded on the experience of others and modified to suit his own apparatus and the limitations of his knowledge of the art.

Practical radiography will teach him vacuum of tubes, opacity of various tissues to x-rays, and the management of apparatus. Failure here is a matter of annoyance and expense alone. Rarely is human life at stake. A working knowledge of dermatology will enable him to observe intelligently the effect of radiation upon the skin, normal or diseased. The wider his knowledge of surgery and pathology, the surer his judgment of the suitability of any given case for surgery alone, x-rays alone, or surgery combined with or followed by x-rays. The broader the man, the better his results will be. A knowledge of electrophysics is a necessity if he would become more than a routine operator. The literature of x-rays is enormous, and much of it worse than worthless, written solely for self-advertisement and betraying ignorance and inexperience.

CONCLUSIONS

(1) Failure must be attributed to faulty technic, not to the agent employed. A gun shoots as straight as it is held.

(2) Identical procedure should produce identical results, other factors being equal.

(3) Experience is better than theory, and both combined are wisdom.

(4) A good agent must never supersede a better. X-rays must not be employed if better results can be obtained surgically with less risk.

(5) Because a man has cured one patient does not prove that he can cure any other similar patient.

(6) The best test of an agent is time.

(7) Unless a man can give enough time to radiotherapy to become expert, he is not justified in holding himself out to the world as a qualified operator.

(8) There is no easy road to success in radiotherapy,—the expert men are the hardest workers.

(9) Radiotherapy cannot be learned from the reading of this or any other paper, any more than operative surgery may be learned by reading alone.

(10) Knowledge of the use of any apparatus does not accompany it, even if it seems to be included in the purchase price.

(11) The man who allows no success or failure to pass until he has satisfied himself as to the exact cause of each, will be able to reproduce his successes and largely eliminate his failures.

(12) A simple, comprehensive, exact record of each case will prove of value more than sufficient to recompense the time it takes.

(13) Good results cannot be expected to follow the use of poor, inefficient apparatus. Tubes, coils, etc., are usually worth about what they cost, and the best are none too good.

(14) Static machines may be used for x-ray work, but they were never designed for this work, and satisfactory measurements of the current generated are hard to make. A machine of this kind may give twice the current one day that it does the next, and thus the dose may vary from day to day. Much good and much bad therapeutic work has been done with them. I have entirely discarded them for every form of x-ray work.

(15) The vacuum of a tube is a difficult subject to master, but results can only be duplicated when the operator has mastered it.

(16) Routine treatment is the rock where many come to grief. The tendency in this direction must be guarded against carefully. There is a constant temptation to give each patient the same length of time with the same tube and distance, regardless of the fact that each patient may require widely different handling.

(17) The dosage must be suited to the case; if it is not, the work of weeks may easily be destroyed in a single sitting. It is better to refuse to treat the patient until another day rather than blindly to expose, with a child-like faith that the ray will do good. It may instead, and likely will, do harm.

(18) In common with every known therapeutic agent, the powers of x-rays may as easily be manifested for harm as good, and equally. What is needed at present is not more x-ray therapy, but more intelligence. There are many things that are as yet unexplained in this work. The use of the rays in many conditions is purely empiric, but they are becoming daily fewer, and less important. The better men in the profession are becoming interested, and some of the best minds in the world have gone in pursuit of these questions. Radiotherapy will soon be reduced to as exact a plane as any branch of therapeutics, and, while many of our present treasured fancies may be ruthlessly demonstrated false and untenable, they will be replaced by truth, supported by evidence exact and incontrovertible. The early demonstrators of every new therapeutic agent have been subjected to much unpleasantness at the hands of the medical world, and radiotherapy has had its detractors who have seen nothing good in itself or its advocates and practitioners; but many of the former detractors have become its warmest friends. Especially is this the case among the members of the surgical profession, who have learned to look upon x-rays in the hands of qualified men as an ally not to be despised in the war upon malignancy. The field of usefulness of this agent will broaden steadily with the lapse of time, and the success or failure of the individual operator will be credited, as they should be, not to the agent employed, but to the skill or lack of skill with which he employs it.

THE ACTION OF METALLIC FERMENTS ON METABOLISM, AND THEIR EFFECTS IN PNEUMONIA

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THE remarks that I have to make in this paper, which concerns the continuation and development of researches carried out together with G. Bardet, and laid before the Academy of Sciences a year ago, comprise facts, on the one hand, and hypotheses on the other. I do not attach much importance to hypotheses, whether or not they turn out to be exact; their only value is that they encourage the worker toward further endeavor. But the facts are so remarkable that they will arouse incredulity in many minds. As I have not the slightest doubt that they will end by compelling belief, through opening out unexpected horizons for therapeutics, I hold myself at the disposal of any one wishing to study, discuss, or refute them.

I

Bredig and his disciples showed that when a small electric current is made to pass between metallic electrodes immersed in distilled water, an unquestionable solution of the metal will be obtained containing per cubic centimeter between 0.09 and 0.2 milligram of the metal used. These same writers found that such solutions possess certain of the reactions of organic diastases, and that these reactions can be either accelerated or inhibited by means of the agents capable of having a similar influence on these diastases.

I have extended this comparison to man. When we inject beneath the skin solutions containing a few ten-thousandths of a gram of a metal, such as palladium, platinum, gold, silver, etc., we observe extensive chemical effects, similar in every detail to those obtained by means of diastases extracted from yeasts. (The solutions of gold I used contained 0.00009 to 0.0002 gram ($\frac{7}{10000}$ to $\frac{2}{10000}$ grain) of metal per cubic centimeter (20 minims). (The strength of the silver solution was about twice as great; that of platinum and palladium less strong.) These effects are:

(1) An increase in urea, which may rise as much as 30 per cent., and attain such a quantity that when nitric acid is added to the urine a noteworthy cloud of urea nitrate is in some cases observed to settle more or less rapidly to the bottom of the glass. This elevation of the urea elimination, of variable intensity, is very common, except in the case of advanced carcinomatous and cachectic patients in general.

(2) An increase in the coefficient of nitrogenous utilization.

(3) An increase in uric acid, which may reach high figures,—as much as three times the initial quantity.

(4) A positive flush of urinary indoxyl.

(5) A decrease in the quantity of total oxygen consumed, without correlative decrease in the carbonic acid gas formed, on which account the respiratory quotient is raised.

(6) A temporary raising of the arterial tension.

(7) These injections give rise to profound modifications of the blood-globules. An injection is followed after several hours by manifest leukocytosis, slight in a healthy person, intense in infectious disorder habitually accompanied by leukocytosis; decrease in the number of leukocytes begins at the end of an hour or two and lasts for a period of time varying between one and two days. It is often replaced by a secondary increase in the number of leukocytes, or else return to the previous condition occurs.

Destruction of the leukocytes is effected at the expense of the neutrophilic polynuclears; at the same time an increase of mononuclears is observed, whose large outlines, carrying out the macrophagic functions, appear in very great quantities. When return to the previous condition or to a normal state occurs, it is not rare to see the eosinophilic function appear or increase. The red blood-corpuscles do not seem to undergo any noticeable modifications; these modifications fall within the limit of mistakes, or they are susceptible of being interpreted in various ways.

II

From the first set of data are deduced the following biochemical consequences:

(1) Experimental confirmation of the celebrated formula given by Armand Gautier to explain the method of vital disintegration of albumin and the formation of urea, apart from any adduction of

external oxygen and by hydration and oxydo-reduction, since the quantity of total oxygen consumed decreases or only increases slightly, while the urea, on the contrary, increases in such a marked degree.

(2) Proof that the indoxyl of the urine is not only engendered by gastro-intestinal fermentation, but that it is witness of the organic processes of hydration and oxydo-reduction.

(3) Proof of the action attributed to organic diastases in the chemical phenomena of disassimilation.

(4) Possibility of assimilating metals in a condition of extremely diluted solutions, compared to these diastases, whence the name *metallic ferments* which I propose for them.

In almost infinitesimal doses, therefore, metals dissolved in water are endowed with very great activity, and, with the exception of certain differences that I shall go into presently, the nature of the metal has but little importance compared to the genesis of the striking physiologic phenomena mentioned above. The same effects can be obtained with the metallic solutions, and particularly with those of copper and manganese, which Trillat has been good enough to prepare for me, and which are obtained by precipitating a metallic salt by means of an alkali in the presence of a colloid substance, such as albumin, gelatin, or gum-arabic. These solutions of manganese and copper have not yet been obtained by electricity, but only by chemistry; those of manganese are more concentrated than the electrolytic metallic solutions—about ten times as strong.

Up to a certain point this extreme division of metals can be compared to the condition of the matter contained in a Crooke's tube. We know that a vacuum creates in the tubes utilized in radiology a peculiar state of matter that the English chemist has called radiant condition, and in which the atoms of the air are widely separated from one another, which renders them capable of simple movements and of exerting their energy to better effect. In the above-mentioned solutions the atoms of the metal, separated as widely as possible, are, as it were, liberated, autonomous in their activity, and susceptible in this way of developing greater energy. It seems as though it is not the gold, silver, palladium, platinum, etc., that act as specific substances, but, indeed, metallic matter in a radiant state, just as takes place in the electric tubes, there being little difference whether the gas is rarefied air or oxygen. The

only real requisite is that the vacuum shall be carried as far as possible, and that the atoms of the gas be at a maximum of separation.

Since I am dealing with hypotheses, why not add that these ideas enable us to form some conception of the action, so uncertain heretofore, of the traces of simple elements combined with organic matter in the living tissues? Armand Gautier has detected arsenic in a great number of our organs, as well as in the majority of our articles of food; iodine is the metalloid of the thyroid body, copper exists in the liver under normal circumstances, manganese in the blood, while iron is recovered in nearly all our elements and tissues, and the most recent research seems to demonstrate the presence of a metal in all organic ferments.

It is not difficult to conceive that these simple bodies, even in the infinitesimal doses in which they are found, are capable of influencing the chemical reactions of elementary nutrition, and this is all we need in order to enable us to raise a small corner of the veil that covers the process of life and to endow with a semblance of shape, however difficult to distinguish, the ancient idea of vital force.

In the same way, the surprisingly energetic action of these metals in extreme dilution enables us to comprehend the remarkable therapeutic effect of certain natural mineral waters, whose compositions did not suffice to explain their action, and in which Garrigou has detected traces of different metals.

And are we not warranted in discussing whether the presence of a metal in extreme subdivision is not connected with many a vital function, and whether this peculiar physical condition of the metal is not one of the intermediaries that connect organic with organized matter, and even with living matter?

III

But let us leave these hypotheses and come to our facts.

Since the principal action of metallic ferments consists, so far as we know, in a stimulation of the hydrating and oxydo-reducing phenomena correlative to a certain number of vital acts, the question occurred to me whether it would not be likely to have a therapeutic effect in cases in which these acts are compromised or insufficient.

For this it was first necessary to determine in what morbid condition this form of metabolism is met with, and thus to settle the effect of these hydrating and oxydo-reducing phenomena in the various pathologic evolutions.

Among these morbid conditions I will only consider pneumonia in this article.

In infectious pneumonia with fatal ending the coefficient of nitrogenous utilization falls on an average to between 68 and 73 per cent., and the output of urea is more or less decreased. In cases that recover, this coefficient varies between 77 and 82 per cent. at the height of the attack. It rises, as does the urea also, a little before thermic defervescence (the precritical discharge), to increase still further during the latter stage.

Since at the same time the total oxygen consumed diminishes and the respiratory quotient increases, as I have shown elsewhere, the result is that crisis in pneumonia coincides with an exaggeration of the hydrating and oxydo-reducing acts, which betray the energy that the system is putting forward in its defence, and that these acts are one of the conditions of this salutary crisis.

The similarity that exists between the chemical phenomena of spontaneous crisis in pneumonia and those determined by metallic ferments, suggested an attempt at some form of functional medication for the purpose of starting, helping, or increasing, by means of these metallic ferments, the chemical acts correlative to the natural crisis of pneumonia.

The results produced by a hypodermic injection of five or ten cubic centimeters of a metallic solution containing from 0.0002 to 0.0009 of active principle per cubic centimeter are chemically very distinct: increase in urea, in the coefficient of nitrogenous utilization, in uric acid, and in free elimination of indoxyl.

Clinically, the thermic defervescence occurs in six cases out of ten before the seventh day. In eight cases out of ten it is abrupt, with a drop varying between 1.6° and 2.5° C. In two cases out of ten it is followed in two or three days by a fresh thermic ascension, which immediately yields to another injection.

The physical signs of the pneumonic lesions show that the disorder continues its evolution in spite of the fall in temperature. The polyuric crisis of convalescence appears to be retarded by a few days.

I have hardly enough cases to justify statistics: out of fourteen

cases treated I have had thirteen recoveries. The patient who succumbed was a man whose defervescence occurred on the sixth day. He had begun to eat and complained of nothing at all, when, on the tenth day, on getting up to have his bed made, he died suddenly. At postmortem large clots were found obstructing the pulmonary artery. The heart was soft, loaded with fat, but without valvular lesions. The lung was still hepatized; the liver voluminous and congested.

Metallic ferments have no action on the pneumonic lesion. They stimulate the reaction of the system against the infectious process and its toxic products. Their usefulness consists in the help they provide to the normal means of defence, since to these vital and personal reactions they superimpose a parallel activity manifesting itself in a quicker disappearance of the correlative symptoms of the infection.

Reduced to this action as an assistant of the *vis medicatrix*, and simply helping nature to cure itself, this functional treatment must by no means be supposed to contain in itself the entire treatment of pneumonia, since it affects in no way the various medications required by the occurrence of some complication, by some abnormal symptomatic predominance, or by the special nature of the lesion itself.

So far as concerns pathologic physiology, it has stood its tests. Clinical experience must now show, when it shall have been used on a large scale, whether it should enter regularly into the therapeutics of pneumonia.

I have used metallic ferments also in a certain number of other infectious disorders, as well as in some diseases of metabolism; but as the results here have not proved as evident as in pneumonia, I shall withhold this part of the subject for a future time. I shall then be able to add to my own researches those undertaken by some of my colleagues.

IV

Before closing, may I be allowed to raise one hypothesis: I have treated 15 cases of pneumonia by antidiphtheritic serum, by the normal serum of horse-blood, by Blondel's lacto-serum, and by reducing-extracts of yeast. I have had 13 recoveries and two deaths, one by pulmonary abscess and pericarditis, the other by pneumococcic nephritis. In these cases the effects of these different

preparations on the urinary reactions and on the temperature were exactly the same as those of the metallic ferments, with a maximum intensity for the antidiphtheritic serum and a minimum for the lacto-serum.

If it should come to be proved by more extensive and profound research that the effects of these sérums and of the metallic ferments on metabolism are identical, would it not be preferable to use the latter in the treatment of diseases amenable to the functional medication by hydration and oxydo-reduction?

The question can also be raised whether the different sérums do not owe, at least in part, their effect to the hydrating, oxydo-reducing diastases they contain; and if this hypothesis were to be verified, we should do well to see whether the oxydo-reducing action of the latter is not also a function of a metal whose nature and proportions we should have to ascertain.

In view of the unforeseen nature, and almost paradoxical appearance, of the facts of this paper, some critics might at first be inclined to imagine that these facts, with the hypotheses that attempt to explain them, belong rather to the ancient metaphysical domain, with which medicine has nothing to do. But I am not of opinion that these researches go to show the existence of any latent healing virtue in a drug, any more than the liberation of this virtue by extreme diluting.

I have been guided by recently recovered physical phenomena (radio-activity, ionization, bringing atomic energy into evidence), and by biologic facts of great importance (action of diastases and zymases, action of divided metals, catalytic phenomena). Consequently, so far from giving myself up to speculation, I have only made an attempt to apply in clinical medicine the new data which physics and chemistry have introduced into science.

My conclusions are:

(1) That metals in extreme subdivision are capable of remarkable physiologic action, out of all proportion to the amount of metal used.

(2) That such metals, acting in doses which therapeutics considered heretofore as ineffectual and useless, by making a profound impression on some of the clinical processes of life whose deviations are connected with many morbid conditions, are probably destined to take an important place among the remedies of functional therapeutics.

THE MUSCULO-TONIC AND DIURETIC ACTION OF FORMIC ACID AND THE FORMIATES

BY HENRY HUCHARD, M.D.

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IN Lémery's Universal Pharmacopœia (first edition, 1697; fifth edition, 1764) is mentioned the use of Hoffmann's *Electuarium magnanimitatis*, a maceration of ants in alcohol, with water and spirit of cinnamon. "This name was given to it," he says, "on account of its valuable properties; it is useful in stimulating the mind, in dissolving and curing cold humors, in exciting the production of semen, and in resisting the action of poison. Its dose is from 1 to 2 drachms." The same book speaks of an *oleum formicarum*, composed of ants and the seed of the *Erusa sativa*; an oil which, when rubbed on the back, perineum, and soles of the feet, "brightened the mind and stimulated the sexual power." Even before Lémery's time, in the Universal Dictionary of James, will be found the opinion of a physician named Hulse (1670), as well as that of Dale, concerning the stimulating effect of ants.

The same tonic and exciting properties of ants were mentioned by Charas in his Galenic and Chemical Pharmacopœia (Lyons, 1717); by Woolden, who advised applications of formic acid diluted with water to hasten recovery in cases of chronic ulcers; and by Ewald, who in his thesis of 1702—*de formicarum usu in medicina*—recommended the use of ants in the form of poultices, of their juice, either pure or diluted, or of a species of oil-maceration, in rheumatic or gouty pain, dropsy, chronic skin complaints, and in paralysis. Patients suffering from muscular inertia received the strange advice to plunge the affected limb into an ant-hill! But later, in 1777, Baumé (Elements of Theoretical and Practical Pharmacy) suppressed all mention of the *Electuarium magnanimitatis*, and only spoke of ant-oil to say that its virtues were illusory, and that its sole effect was due to the olive oil.

The memory of these statements has not completely died away in Switzerland and Germany, and formic acid, prepared chemically,

as well as the extract of ants, are still pharmaceutical preparations in these countries, where, it is said, they are highly thought of for rheumatism and gout. In 1885 Schulz recommended the antiseptic action of formic acid, and in the same year Kocwacs reported that it was an undoubted stimulator of the nerve centers and motor nerves. In the opinion of the latter writer formic acid is a vaso-constrictor, while sodium formiate is a vaso-dilator; finally, the latter salt is diuretic in dropsy without renal lesions.

In France the acid, extracted at first from the red ant as long ago as 1669 by Fisher, of Sheffield, had disappeared from the pharmacopeia. It had been almost entirely forgotten, in spite of Ravier's thesis (Paris, 1822) on the use of formic acid in chronic rheumatism, and, although its first synthesis was effected by our great chemist, Berthelot, other processes have since been devised by a variety of other chemists.

Still, formic acid and the formiates have been recommended during the last few years by Garrigue in the treatment of infectious and chronic disorders, and even as a curative treatment of cancer and tuberculosis. As yet, however, this result has not been demonstrated; we must wait patiently for further proof, and my remarks to-day do not bear on this aspect of the question.

But in Garrigue's book (1902), in which his enthusiasm, no doubt excessive, led him to hope for the cure of cancer and tuberculosis, the following passage will be found concerning injections of formiates on himself: "This result was rapid, and my appetite quickly increased, as well as my physical and cerebral activity." This remark is exact, but this mere mention did not suffice to call attention to the real properties of formic acid and the formiates.

Clément, of Lyons, then published a report on the action of formic acid on the muscular system, which I presented to the Academy of Medicine in July, 1904; and the present paper deals merely with the really remarkable musculo-tonic action of formic acid and the formiates, and with their diuretic effects.

The foregoing short historical review shows that this is an old remedy that has become new to-day because it had been too long forgotten.

MUSCULO-TONIC ACTION

This oblivion was unmerited, for extensive clinical observations and very exact experiments have now shown that formic acid in-

creases muscular strength in proportions that may be as much as fivefold, that it augments the activity of the muscles and their resistance to fatigue, and that it acts on the entire muscular system, both on the striated and on the unstriated fibers. "A person making use of formic acid," says Clément, "soon feels more strength, vigor and activity; he moves without trouble; he no longer apprehends effort or work; he no longer experiences the well-known weariness on awakening; and he is better able to withstand heat and cold. In short, every exhausting cause that induces physical languor or a tendency to bodily inactivity has less effect on him. After two years of close observation, I maintain my affirmation, however venturesome it may seem, that a normal person, with normal diet, performing normal work, no longer feels fatigue so long as he makes use of formic acid."

To read such unexpected claims leaves one at first with a certain feeling of incredulity; but this impression disappears in the light of the tests that I have been making for four months with the constant and untiring assistance of my two interns in medicine and pharmacy. I shall not bring forward as evidence either subjective sensations or results furnished by the dynamometer, as they are too open to criticism and discussion.

And yet, the sensations felt by patients can be mentioned, since, in most cases, and of their own accord, they speak of feeling very well, while their movements are freer and stronger than usual; yet they were not warned about the usual effect of the drug.

Again, I have about thirty case reports in which, in various diseases, sodium formiate had a most favorable action on the course of the disorder. Thus a woman of 75 years, with serious catarrhal pneumonia and severe prostration, was given sodium formiate in doses of 3 grams per diem and recovered. My colleague at Necker Hospital, Dr. Hirtz, whom I had asked to try this remedy in his wards, spoke to me of three cases, one of which concerned a woman of 85 years, with influenza and pulmonary congestion at both bases; sodium formiate (2 to 3 grams per diem) promptly stimulated her muscular strength and appeared to hasten her recovery. But I will not cite any more of these cases, where longer experience is required, as it is not on them that I wish to base my argument.

Among Clément's experiments, for it was he who brought into evidence the musculo-tonic action of this drug, let me cite the fol-

lowing: After using formic acid his patient was able to furnish ten periods of work, instead of five as before the drug was used. During these ten periods the man registered with Mosso's ergograph 479 elevations of a 5-kilo weight, instead of 132. The total work accomplished amounted to 106 kilometers, whereas before the formic acid was given it had only been 21. The work effected after the formic acid was, therefore, fivefold.

The effect is felt quickly, inside of 24 hours, and a number of persons to whom formic acid or sodium formiate was administered in the doses to be mentioned further on, remarked of their own accord that they felt stronger and more "fit" in ordinary walking, stair-climbing, and hill-climbing, and that their sensation of fatigue was lessened or retarded.

This effect on the muscular system is fairly lasting, and continues for 8 to 10 days after the drug has been taken. Under its influence the painful sensation caused in muscles by repeated contractions is very noticeably lessened, while the tired muscles quickly recover their energy. The musculo-tonic action seems to affect as well the heart and the vessels, the gastro-intestinal tunics, the diaphragm, the bladder muscle, so that the power of urinary emission is much increased,—in a word, all the muscles, striated or unstriated, of the body. The circulation is improved and the arterial tension is raised in cases in which the myocardium is weak, whereas it is lowered when there is hypertension due particularly to disordered peripheral circulation. Formic acid also increases the tonicity and contractile power of the laryngeal muscles, as well as of all the respiratory muscles: whence an increase in voice-power from which singers may derive advantage; whence also greater amplitude in breathing and marked decrease in loss of breath produced by effort and running; whence, finally, visible awakening of appetite and quicker digestive evolution in gastric hyposthénia with or without dilatation.

The foregoing are the remarkable effects attributed by Clément to the musculo-tonic action of formic acid and the formiates. As I possess possibly less enthusiasm than he, I have not been able to verify nor confirm all of them. Thus, making use of Dupont's spirometer, I have not found that the respiratory capacity of persons under the formic treatment is appreciably increased; I have not noted an increase in arterial tension, rather a decrease, due, pos-

sibly, to the vaso-dilator properties of the formiates. But the manifest musculo-tonic results I have obtained during the last four months in collaboration with my intern, M. Mougeot, enable me to believe in the importance of this medication, which I have already used in different morbid conditions: neurasthenia, diabetes, asthenia from influenza, the adynamic state in infectious disorders, convalescence, anemia, hyposthenia with dilated heart, gastric hyposthenia, senile debility, and the weakness due to an exclusive milk diet. It is possible to foresee the favorable effect it will have in all kinds of sport and muscle-training, in marching in armies, in fact, in all instances where it is desired to increase resistance to fatigue.

Among the many cases I possess, both in hospital and private practice, and relying on the data supplied by Mosso's ergograph, let me report the following:

A male nurse in my wards, healthy in all respects, took 3 grams of sodium formiate per 24 hours. Before doing so his muscular strength was represented by 6 kilogrammeters; the next day it was 7.75, and on the following days 7.56, 7.45, and 7.05, after a night on duty, when he had only 4 hours' sleep in 24 hours.

A patient, 49 years of age, with torpid tuberculosis in the first degree, took 3 grams of sodium formiate per diem for a week; her muscular strength rose from 3.08 kilogrammeters to 5.64, 7.275, and 8, and three days after the drug had been stopped it was still 5.50.

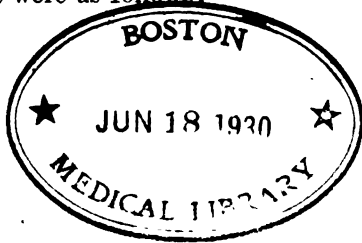
In a young Italian physician attending my wards, the muscular energy rose from 4.56 to 4.90 kilogrammeters after the administration of sodium formiate, in spite of an attack of influenza.

A woman of 53 years, suffering from arrhythmic arterial cardiopathy, found her muscular strength rise rapidly from 2.32 kilogrammeters to 4.05 after a single dose of 3 grams of sodium formiate.

Another woman of 49 years, with chronic nephritis, was put on the same treatment. Her albumin decreased noticeably, while at the same time the diuresis increased in quite large proportions.

On the other hand, no result at all was obtained in a woman of 23 years with mitral regurgitation.

I experimented on myself and on several of my students. The results were as follows:



Dr. Triedel:

Before taking the formiate	5.70 kilogrammeters.
First day after taking it	9.60 "
Second day after taking it	9.35 "
Third day after taking it	9.05 "
Fourth day after taking it	10.70 "
Fifth day after taking it	11.50 "

M. G——, extern of the wards, 8.850 before the formiate. After the formiate, 8.875, and two days later, 10.275.

Dr. Huchard:

Before taking the formiate	9.90 kilogrammeters.
After the first day (2 grams of formiate).....	8.750 "
After the second day (2 grams of formiate)...	20.625 "
After the third day (4 grams of formiate)....	20.975 "
After the fourth day (4 grams of formiate)...	20.200 "
After the fifth day (3 grams of formiate)	30.650 "

Consequently, after 15 grams of sodium formiate taken during five days, my muscular strength rose from 8.75 kilogrammeters to 30.65, an increase of nearly four times in a space of six days. I stopped taking the drug to see whether there might not be a source of error consisting in the accumulation of doses; but in several of the cases above mentioned the ergographic tracing descended progressively and regularly during the five or six days that followed the giving up of the remedy, and on the ergograms that concerned Dr. Triedel and myself the cessation of the remedy was also followed by the almost gradual diminution of muscular strength. We clearly noticed that the muscular contraction employed in the use of the ergograph became more painful when the drug had been suppressed, a fact that has its importance, as we shall see further on, in explaining the physiologic action of the drug.

During the two days after ceasing the sodium formiate my muscular strength fell from 30 kilogrammeters to 19 and 18, and for the three following days it oscillated between 14 and 17. In Dr. Triedel's case it fell from near 12 kilogrammeters to 9, 10, and 7 during the first five days after stopping the drug. These experiments have only just been made, but it is our intention to carry them on longer, in order to ascertain the real duration of the increase in muscular strength.

It is very evident that very serious objections can be made to all these experiments; but so far from wishing to avoid them, I shall be glad to have them made. The management of the ergograph, for instance, requires a certain amount of habit and a very precise comprehension of the movements to be effected; it is also a delicate instrument, and subject to certain errors. But, the many sources of error being eliminated, one fact remains clearly proved by my experiments, which confirm those of Clément: the musculo-tonic action of formic acid. We have not yet clearly established by means of the ergograph the muscular strength per unity of time, and it would no doubt have been preferable to choose for our experiments persons unaware of the musculo-tonic action of the drug, persons free, consequently, from all auto-suggestion capable of determining temporary increase of muscular strength under the mere influence of will-power. We hope to continue our investigations, while seeking to set aside all cause of error. But, I repeat, one fact remains demonstrated: the musculo-tonic action of formic acid. This probably explains the activity, strength, vigor, and endurance of certain working insects, caterpillars, and particularly ants, which are able to carry loads out of all proportion to their size. This fact becomes comprehensible when we think that ants possess and secrete formic acid in abundance, a generator of strength. The presence of this acid in the glands of the nettle plant, in tamarind fruit, as well as in pine-needles, etc., explains also the vogue of certain remedies formerly drawn from these vegetables. Even agriculture makes use of the stimulating properties of formic acid; to hasten the germination of seed a solution of formic acid 1 to 1000 has been employed. The seed is watered with this preparation, and, instead of germination, beginning in ten days, as is usual in summer, it has been found to occur much sooner, in two or three days.

DIURETIC ACTION

Another very important action, hardly mentioned by writers on the subject, but which has appeared unquestionably in almost all of our cases, is the effect of formic acid on diuresis. The urinary secretion is rapidly and very markedly increased with the three following salts, with which we have experimented, the formiate of lithium, sodium, and potassium. Sodium formiate is, however, the one we have most frequently used.

To begin with, it would be interesting to know what becomes of the formiates when introduced into the human system, and to study their mode of elimination and their action on urinary secretion.

According to Rabuteau, sodium formiate, and no doubt all formiates, are changed into bicarbonates in the system. But such is not the opinion of Gréhant and Quinquaud, who proved that sodium formiate introduced into the digestive tract or injected into the blood passed mostly into the urine without undergoing decomposition,—thus: they injected into the jugular vein of a dog 20 c.c. of distilled water containing 4 grams of sodium formiate; the urine collected 48 hours later gave 453 c.c. of CO, corresponding to 2.22 of formiate. Two days later 40 c.c. more of CO were obtained, equalling 0.27 of formiate, making a total of 2.49 of formiate eliminated by the urine, which continued to show traces of this salt the following days. Other experiments showed them that this urine did not contain an excess of carbonates. The conclusion is manifest: that most of the formiate salt passes into the urine without decomposition, and this has been confirmed by my intern in pharmacy.

These experiments further showed that formic acid appears in the urine about a quarter of an hour after an injection of formiate. The first urine passed is always thick and slightly alkaline, and contains more formiate than that which is passed later: 0.13 per 100, as against 0.07, 0.06, and 0.04. After the third or fourth time the urine becomes transparent and acid once more.

The elimination lasts from 4 to 6 days. If, for instance, 3 grams of formiate are taken in 24 hours, 1.60 grams are eliminated in the first 48 hours, 0.28 gram during the two following days, a few centigrams during the next two days; on the seventh day it can no longer be detected. With larger doses, 4 to 5 grams of formiate per diem, the elimination lasts somewhat longer, up to the eighth day.

The ratio between absorption and elimination is fairly constant, to judge by three experiments: 62 per cent., 59 per cent., and 66 per cent., an average of 62 per cent.

The diuretic effect is very evident; it is produced rapidly the first day, and disappears a day or two after the drug is discontinued. The following figures will demonstrate this action: In a woman of 56 years, with mitral stenosis, the volume of urine, which before the experiment was 750 c.c., rose to 3000 c.c. after 1 gram of formiate of lithium, and to 4000 with 1.50 grams of the same salt.

When the drug was discontinued the volume of urine decreased progressively to 2500 c.c., and finally to 1500 c.c.

In a woman of 52 years, with early renal sclerosis and albuminuria, the urine from 1000 c.c. rose to 2700 after 3 grams of sodium formiate for four days, and descended to 1250 c.c. when the medicine was stopped. The albumin had then almost entirely disappeared.

A man of 49 years, with tuberculosis in the first degree, showed 2500 c.c. of urine per 24 hours before treatment; after 3 grams of formiate of sodium, 3750; on ceasing, 2550; after 3 grams of formiate of potassium, 3700 to 4000; three days after ceasing, again 2400 c.c.

A healthy woman of 36 years. Before the test 1250 c.c. of urine; after 3 grams of formiate, 2250; on ceasing, 1100 c.c.

I have about 20 other cases that demonstrate the diuretic action of the formiates. But this effect seems less constant than with theobromin. In any case, however, if further tests confirm not only this diuretic action, which seems undeniable, but also the attenuating effect on the amount of albumin, we shall possess in the formiates a remedy of use in the treatment of renal disorders and of arterial cardiopathic cases.

From the details of these cases we find that in the majority of instances there is a greater elimination of products of disassimilation. This increase is particularly noticeable for the urea, which, more than the other elements, rises under the effect of the formiate. Uric acid does not seem to be eliminated any more freely than without the drug. The nitrogenous ratio always rose in our cases, proving better utilization of nitrogenous material, more active nutrition, under the influence of the formiate. Finally, the urine acidity always decreased and sometimes disappeared, the first urine passed being always alkaline.

TOXIC ACTION

I requested M. Eréhart to make experiments with a view to ascertaining the degree of toxicity of the formiates, and, as will be seen by the reply he has made, this salt turns out to be very slightly toxic, which I had already inferred from my clinical and therapeutical observations, which also agreed with those of Clément. Eréhart has not yet found the fatal dose for mammiferæ, and only by operating on frogs 30 grams in weight has he obtained positive results.

Eleven grams of pure sodium formiate were injected into the circulation of a dog weighing 11 kilos. In a quarter of an hour mucous vomiting occurred. No other symptoms manifested themselves; the animal walked, and returned without difficulty to its kennel. Subsequently the dog remained in good health.

A rabbit weighing 2.5 kilograms: 10 grams of sodium formiate were injected into the stomach inside of three minutes. No symptoms occurred, although the dose was 4 grams per kilogram of weight.

With a dog of average weight 60 grams were necessary to produce death; consequently, the toxicity of the formiates is insignificant.

DOSES

First, a few words as to the physical properties of the formiates.

They are prepared by saturating the acid by carbonates or oxids. Sodium formiate (a white salt, crystallizing in rhomboidal prisms), which should be used in preference, is very soluble in water and is deliquescent, for which reason it cannot be given in wafers. The formiates of potassium, ammonium, lime, lithium, and iron are soluble in water, whereas the formiate of lead is only slightly so, and that of mercury absolutely insoluble.

Sodium formiate, in the doses to be mentioned, has so far not given rise to gastric intolerance. Formiate of lithium, which I have also used, should be given in smaller doses than the sodium salt (1 to 1.5 grams per diem, instead of 3 to 4), because it readily induces nausea and vomiting. Formiate of potassium should be given in the same dose as the sodium salt: 3 to 4 grams a day, 1 gram at a time; it appears to have a more marked diuretic effect than the sodium formiate.

Care must be taken not to prescribe the formiates in acid syrups, whereby a certain quantity of the formic acid may be set at liberty and irritate the stomach.

The dose of formic acid for an adult is about 2 grams; it should be diluted in about half a glass of water and neutralized with 4 grams of sodium bicarbonate. But this preparation, which was recommended at first by Clément, is unpleasant to take. It is preferable to begin at once with the sodium formiate, 3 to 4 grams a day, dissolved in water and aromatized or sweetened with Curaçao

or syrup of bitter orange. The most agreeable prescription I have found is:

R	Sodium formiate	4 drams	16
	Syrup of bitter orange	8 ounces	250

M. Sig.—One tablespoonful (15 c.c.) three or four times daily.

I have not yet tried hypodermic injections.

The system does not seem to become accustomed to the drug, so that it does not lose its effect after continued use, and from using it himself for 20 months Clément is able to say that the remedy is harmless. It has no ill effect on the kidney.

The physiologic action of the formiates is a question still under discussion. We know that its musculo-tonic effect is far greater than that of testicular extract or of ibogaïn, which appears to be a tonic rather of the nervous system; but we do not yet know the physiologic mechanism of this remarkable musculo-tonic effect. Clément thinks that the drug possibly acts by favoring muscular interchanges, the protoplasm, under its influence, making better use of the glycose and freeing itself more rapidly of waste products; the latter may even be entirely transformed by the formic acid.

Personally I am inclined to believe that the formiate acts largely by inducing a certain degree of muscular anesthesia and by lessening the painful sensation of muscular fatigue. This fact seems to me proved by the disappearance of this pain in the muscles acting on the ergograph as soon as a certain quantity of formiate has been absorbed.

Whatever the truth may be as to these explanations, the points that can no longer be denied are the musculo-tonic and diuretic action of the formiates, the importance of this means of treatment, and the manifold therapeutic applications which our experiments and cases appear to have definitely established.

THE SYMPTOMATIC TREATMENT OF TUBERCULOSIS

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MOST physicians are cognizant of the mass of recent literature dealing with general and special phases of the treatment of tuberculosis—a preventable and much dreaded disease. My justification for discussing the symptomatic treatment is found in the fact that in many excellent treatises intended for the education of the profession and the people, this subject, of pronounced importance to the practitioner of medicine, is almost wholly neglected. Almost every article elaborates upon the hygienic, climatic, dietetic, and other forms of therapy, and concludes with the stereotyped expressions, “treat symptomatically,” “meet the indications as they arise.” To say to treat a hemorrhage, cough, or night-sweat symptomatically may relieve the mind of the writer by the early dismissal of his subject, but when brought face to face with an emergency he may have some curiosity to know just what that symptomatic treatment is.

Anemia, first alphabetically, is often first symptomatically for our consideration. Be this a pretuberculous state resulting from inanition or a tuberculous sequel, the indications are the same. Good food, fresh air, sunshine, regular habits, and sleep are the best tonics; but these can be and often must be assisted by properly selected medicines.

To ascertain positively the remedy suitable for each individual patient, an adequate examination of the blood should be made. In oligochromemia we know that iron should be given in some form, and the patient's stomach and idiosyncrasy must be considered. Ordinarily pills of ferrous carbonate will be kindly received. One 5-grain (0.3 gram) pill three times a day, increased to three pills three times a day, is convenient and effective. In oligocythemia, arsenic in the form of solution of potassium arsenite, in increasing doses, usually increases the number and character of the red blood-corpuscles. In the more obstinate anemias phosphorus, alone or combined with other tonics, has been yielding excellent results.

Phosphorus is an element in the economy absolutely essential for healthy metabolism. Children minus this element are weakly and rickety, susceptible to extraneous influences, and possess little or no resistance to infections. The nervous system and glandular structures are abundantly supplied, and its presence in every tissue and fluid emphasizes the importance of phosphorus in the nutritive process of the body.

The affinity of phosphorus for oxygen leads us to regard the former as the oxygen receiver, the element greatly consumed in tissue combustion. The two elements, oxygen and phosphorus, are the real fuel for nerve energy, anabolism, and catabolism. Functional activity depends upon nerve force, and every cell must exert energy requisite for extracting from the blood elements necessary for its maintenance and propagation.

The amount of phosphates eliminated in the urine is regarded as an index to the extent of tissue combustion. However, we must first determine if the excess depends upon the diet, by computing the proportion of phosphoric acid to the nitrogen compounds ingested. If the excess of phosphates in the urine depends not upon the food, we have a true phosphaturia. Continued phosphaturia must consume and exhaust its phosphide element, and normal vigor and resistance are lowered.

This is the condition we have in some of the exhausting diseases,—diabetes mellitus, tuberculosis, and various bone diseases, in which phosphaturia is always present. From this survey the administration of phosphorus in some form is not only rational, but imperative, in the successful combating of tuberculous anemia. In appropriate doses it promotes constructive metabolism, increasing the activity and resistance of every structure and cell in the body.

The hypophosphite salts are possibly the most desirable form for administering phosphorus. Some advocates of the hypophosphite treatment of tuberculosis insist that most pronounced benefit is obtained by giving the salts singly, as each salt has its peculiar property. Thus the sodium salt is recommended in apyretic cases or in the infiltration stage when expectoration is scanty; the calcium salt when there is too free expectoration and a tendency to too rapid breaking down of tissues. When the excretions are checked the sodium salt is resumed. The quinin salt is used temporarily when the temperature is over 100° F.

Personally, I have used the compound salts with the glycerin vehicle, believing the phosphorus was accountable for the results. Quinin and strychnin may be added when needed, the former being a general and bitter tonic and intestinal antiseptic, the latter our best nerve and muscle toner, and most constant and reliable respiratory stimulant.

It is well to have in mind the conditions that limit the pushing of hematonics. When a patient has been consuming his own tissues, a rapid increase in the amount of the blood and in the force of the circulation has a tendency gradually to distend weakened and impoverished vessels and rupture those softened by the process of inflammation and suppuration. As a result, we have hemoptysis and further disintegration of tubercular deposits.

Anticipating this issue, the vessels should be toned for the reception of increased force, and for this purpose ergot is of value. By toning these relaxed vessels in the lungs the circulation is improved and the stagnant blood interfering with oxidation is pushed on, aerated, and made to perform its vital duty. Vascular stasis throughout the system is greatly improved by the judicious employment of this drug.

This brings us to one of the most frightful symptoms these patients develop. Hemoptysis is sufficient to alarm the patient, his relatives and friends, and when it develops into a copious hemorrhage even the attending physician is in no enviable position.

Hemoptysis, even of the most trivial character, should never be passed by lightly, for the pinked and streaked sputum of to-day may be the precursor of an alarming hemorrhage to-morrow. Treatment, if neglected previously, should be instituted at once to tone these weeping vessels and membranes.

A hemorrhage is often of greatest benefit in washing out an abscess, since if the rupture had occurred in any direction other than into a wind-tube, it might have scattered the tubercle bacilli throughout the lung.

In the treatment of hemorrhage from the lower air-passages rest is of paramount importance—rest to mind and body. The clinical picture of a pulmonary hemorrhage, with all its tragedy, is familiar to most physicians. During the period of excitement and anxiety the heart is pounding away with all the vim and vigor such occasions can produce, and the bleeding vessels are kept open by the increased force and blood-pressure.

Here is where the trusted physician, simply by his presence, quiets a fretful tempest, for often, in spite of his medication, the hemorrhage ceases.

Let us consider the conditions we wish to produce and then apply the remedies we know will assist in bringing about these conditions. First, we must have absolute mental and physical rest; second, we must reduce the force of the heart and lower blood-pressure, to permit of a clot forming in the bleeding vessels; and, third, we must keep this clot from being disturbed and favor healing of the wound.

The first indication is met by placing the patient in recumbency and removing all irritating or exciting elements. Ice-pack to the chest and small pieces of ice in the mouth assist in quieting the heart and occupying the mind. In some instances morphin and atropin hypodermically are needed to relieve nervousness, coughing, and straining. In extreme cases the extremities are to be tightly bandaged, the patient brought to the edge of the bed, face downward, and the chest inclined to favor the expelling of the blood from the lungs. When a patient is drowning in his own blood he must be encouraged to cough it up and remove the clots that are hindering the entrance of air.

The second step of this treatment begins immediately the patient is recumbent. Amyl nitrite by inhalation promptly lowers blood-pressure, and in many instances the hemorrhage ceases at once. If vascular dilatation must be continued, nitroglycerin or erythrol nitrate can be depended upon. If the heart continues too vigorous, aconite will reduce the force and rate and assist in lowering blood-pressure.

The third requirement is of no less importance. How often have we seen hemorrhage break out anew after a bowl of hot broth or a cup of hot tea. Conjoined with continued rest for a week we must insist upon a cold diet and a laxative effect of the salines.

I have had patients upon an almost exclusive diet of gelatin and cream for several days after a hemorrhage, and believe that if given in large quantities gelatin will assist in preventing a recurrence. Cases are reported in which the hemorrhages resisted all other treatment, and were stopped by injections of gelatin. But the fact that most of the early hemorrhages stop of their own accord, like the vomiting of pregnancy, gives credit to the last-used medicinal agent.

Some of the fallacies in the treatment of pulmonary hemorrhages can be mentioned in brief. Local hemostatics rarely if ever reach the spot, and inhalation of vapors increases respiratory effort, and is, therefore, harmful. Hemostatics internally cannot be given in amounts large enough to have any effect, even if the astringent action was not lost before the bleeding point is reached. Suprarenal extract, digitalis, ergot, hydrastis, strychnin, and salt solution all increase the blood-pressure, and are, therefore, contraindicated.

In cases of collapse, atropin and strophanthus should be tried before resorting to strychnin. The former has a sedative action upon the respiratory mucous membrane and assists in keeping the peripheral vessels dilated; the latter, while strengthening the heart, does not contract the blood-vessels.

It is well to remember that a physical examination at this time is as much out of place as gymnastics or hill-climbing; that blood in tied-off extremities should be admitted slowly; that recurrence of hemorrhage may be excited by severe mental or physical exertion, shouting, singing, hot or stimulating drinks, dust, or overheating. A trace of blood in the sputum, sharp pains in the chest, or tickling in the throat, indicate a return to complete rest, cold foods, and laxatives. Exercises and lung stretching should not be attempted for some weeks, and then must be graduated and always moderate.

Cardiac weakness requires rest and watchfulness. Everything that would disturb the tranquillity, mental and physical, should be avoided. When not associated with hemorrhages, strengthening by graduated exercises should be practised. Strychnin and strophanthus are useful at times; in cardiac excitement, rest and ice (a bag or coil) to the pericardium.

Dyspnea may be associated with heart weakness or general muscular weakness, in which event, if the patient has recuperative powers, out-of-door and graduated hill-climbing may be of some benefit. When due to exhaustion and lessening of lung space the need for more air should be reduced by rest. In extreme cases the administration of oxygen is of great comfort, and in the last hours a real blessing. When dyspnea is due to glandular pressure, spasmodic stricture, or viscid secretion, pills of ferrous iodid, one, two, or three times a day, are of service, and should be used in preference to potassium iodid.

The *cough* very often receives more consideration than the

patient, and it is nothing short of remarkable how some of these patients can survive the nauseating mixtures they swallow daily. The cough is a necessary aid to the elimination of poisonous inflammatory exudates, and if the cough be stopped in a well-established case with copious exudation, the patient deteriorates rapidly.

The cough should be let alone, unless it is troublesome, persistent, and disturbs the patient's rest. Violent coughing should never be permitted for fear of hemorrhage or the breaking down of protective membranes and dissemination of micro-organisms. The cough that takes all the nerve out of the patient, keeping him depressed and worried, should be relieved.

For simple reflex, pleural, bronchial, pharyngeal, or nasal-irritation cough, with little or no secretion, codein should be given often enough to control. The cough does no real good, and does harm by exaggerating itself. In catarrhal conditions of the air-passages, enlargement of lymphatics, thick and boggy mucosa, syrup or pills of ferrous iodid will give most pleasing results. This preparation seems to meet the plan of reducing inflammation, promoting removal of morbid secretions, and destroying the germs. Especially when the cough is hard and frequent, in exhausting paroxysms, the mucus, tough and tenacious, often producing vomiting, the ferrous iodid softens, liquefies, and removes these inflammatory products that are perpetuated by their own presence.

Tracheal injections and vapor inhalations are useful if persisted in. A nebulizing formula I have used with pleasing effect is as follows:

R	Eucalyptus	3
	Tereben	3
	Chloroform	3
	Oil of sassafras	1
	Menthol	0.4
	Liquid petrolatum sufficient to make	100

Cleansing of the air-passages in the morning is important. A gargle of hot water and salt, or, in some instances, cold water, is effective; better still, or rather, in addition, a brisk walk in the open air. The patient can then relish his breakfast, and stands more chance of retaining it.

The consumptive must learn to control an empty cough that

only excites other paroxysms. Thus he can be trained to cough only when it is needed to remove secretions.

He should avoid gases, dusts, and irritants, and, above all things, oil or gas stoves. The many demulcent drinks and lozenges are too expensive to the stomach to be recommended. Counter-irritants or the plaster binder may be of assistance when the cough is due to pleurisy.

Pain is usually due to involvement of the pleura, and can often be benefited by applications of mustard or iodine in some form. The application of glycerin and clay mixtures act by confining heat and restricting respiratory movements. The osmotic action of glycerin when applied to the chest is a decided stretch of imagination. As glycerin is readily absorbed when rubbed into the skin, it makes an excellent vehicle for belladonna and iodine in these cases.

The pleuritic effusions serve to relieve these friction pains, and moderate effusions, doing no harm, had better be left alone. If dyspnea and fever become more pronounced and the heart embarrassed, it becomes imperative to remove the fluid at once. For the neuralgia and muscular pains, moist, warm applications may be used with those already suggested. Menthol or stimulating liniments are beneficial, especially if the rubbing is vigorous. An application I have found of value is as follows:

R	Tincture of iodine		
	Chloroform	of each	10 0
	Methyl salicylate	sufficient to make	100 0

M. Sig.—Apply on soft linen under oiled paper.

As a last resort, we can give antipyrin, the salicylates, opium, or some of its derivatives.

Fever may be present long before a physician is consulted, and always bears relation to the inflammatory process in the lung. If the process becomes inactive from time to time, the fever for a corresponding time abates. Writers generally advise putting these fever patients to bed, to which practice I will venture to take some exceptions.

We all know that the consumptive, as a rule, supports a high temperature with little or no annoyance. Frequently patients have come to my office with a temperature ranging from 101° to 103° F., expressing themselves as feeling good, but that they need to stay

out of doors, since the moment they go indoors the fever comes on. Now, this fever may not be a bad thing if it is true that the germicidal powers of the blood are increased when the temperature is above normal; and if the tissues can react promptly from the daily absorption of ptomaines, an agglutinative power and immunization is established that will assist in combating the disease. However this may be, the objection I will make to placing pyretic patients to bed is: (1) The length of time these patients must be confined if there should come a period of three days when the temperature remains normal; (2) air and sunshine, so important in these cases, is in a measure lost; (3) anorexia and insomnia are almost certain to follow, and two other great aids to recovery are lost; (4) depression comes next, and hypostatic congestion and bed-sores sooner or later develop; (5) in the extreme cases in which recovery ensues, it is not those that take to their beds, but those that shoulder a gun and take to the woods who are restored to health.

I have under observation pyretic patients who relapse when confined to the house or bed for a few days on account of inclement weather, and who when permitted to go about and live out of doors improve in every respect, even making substantial gains in weight.

It occurs to me that most of these patients are injured by confinement to a room or a bed. There are patients, however, that require treatment for this symptom, and absolute rest in bed is required, but never continued longer than absolutely necessary. When a patient will hold his own or gain a little weight, an out-of-door life will develop an appetite and produce better sleep, even if he has an elevated temperature every day. In treating these fevers, that are fatiguing to the patient, rest and the cold coil or ice-bag to the head is all that is usually required. The chill should be anticipated with warm blankets and hot toddy or wine. Atropin or nuxvomica might be useful at this time, and will assist in preventing the sweat that follows.

For the *night-sweat* there is nothing like a cold room with an abundance of fresh air. Drugs are not often needed, and some previously employed have the same action as the pan of water under the bed. A glass of diluted top milk and a few crackers before retiring often act like a real antisudoral. Night-clothing should be light and warm. Pajamas should be worn to keep the surfaces from coming directly together. The gradually cooled shower-bath is an

excellent measure for toning the skin and circulation. Vigorous rubbing with a bath-towel and drawing of the skin assist in preventing skin leaking, and should always follow the bath.

When the sweat does occur, the clothing should be changed. In fact, another bed should be at hand. Sponging with a solution of alum and capsicum, the latter especially when the skin is cold and clammy, is sometimes of apparent benefit.

Of the drugs prescribed, atropin gives most universal results, although the throat dryness is always disagreeable, and cerebral symptoms may be pronounced. A combination I have used with some success is as follows:

R Atropin sulphate	0 005	$\frac{1}{12}$ grain
Agaricin	0 05	$\frac{1}{2}$ "
Picrotoxin	0 01	$\frac{1}{4}$ "

Mix, and make ten pills.

Sig.—One or two pills on retiring.

When the atropin is objectionable the following may be substituted:

R Extract of nux vomica	0 08	$1\frac{1}{2}$ grains
Extract of ergot	3 0	50 "

Mix, and make ten pills.

Sig.—One or two pills on retiring.

For *insomnia* the hypnotics are not often needed. Mental rest and open-air life are the first remedies.

For *digestive disturbances*, open-air life, hydrotherapy, and dietetics are useful. Dietetics being a special department of treatment, I will simply state that it makes little difference as to the variety of food so that it is abundant, nourishing, and not too difficult of digestion; but the manner of eating is important. Eating dry requires more thorough mastication and, therefore, more complete mouth digestion. After the meal and between the meals is the time for drinking. We should avoid overfeeding, rapid feeding, and syrupy mixtures that disturb the digestive organs. Digestives and sedatives should be given only when needed.

Diarrhea should be met with guaiacol carbonate, calomel, wines rich in tannin, and food with little residue.

Last caution, keep on good terms with the stomach, and do not give a medicine for every symptom.

OPOTHERAPIC TREATMENT OF RENAL INSUFFICIENCY

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WHEN the subject is considered as a whole, the means we daily use in treating serious uremia, the final stage of complete renal insufficiency,—whether we endeavor to arouse the renal eliminatory function by means of diuretics or cardiac drugs, or to bring into play certain alternate functions by the use of purgatives, sudorifics, or, lastly, by the more radical methods of blood-letting or lumbar puncture,—these means, in spite of their apparent diversity, all aim at the same exclusive object: to moderate toxemia, the obligatory result of glandular impermeability, by facilitating the elimination of the retained poisons through the agency of the natural emunctories, or by endeavoring to withdraw them directly from the blood in circulation.

It was, therefore, natural to inquire whether we could not do better, or more, with our therapeutics,—that is, neutralize these poisons directly in the blood or in the tissues impregnated with the toxic edema; whether, in a word, opotherapy, sprung from Brown-Sequard's memorable researches on internal secretions, applied systematically to the treatment of Bright's disease, might not be able to effect this result. Now, we do not consider that renal opotherapy has fallen short of our expectations. The reason why it has not yet entered into our ordinary practice is that we were inclined to demand greater results from it than it is capable, strictly speaking, to give. On the other hand, experience has shown us that, when used at the proper time and under clearly defined conditions, it has unquestionable indications and efficacy. To-day I wish to consider what conditions warrant its use, what hopes we can found on it, and in what way it can best be put into practice.

Three different methods have been followed in endeavoring to compensate the failing renal function and to replace the suppressed internal secretion.

I

Renal opotherapy was first instituted with a glycerin extract of kidney tissue in a case of uremia that had reached the final coma, in which, consequently, nothing but transitory improvement could be hoped for. This extract was prepared by macerating for five hours, in a vessel set in ice, 200 grams of the cortical substance of an ox-kidney finely chopped and mashed in 300 grams of glycerin and 280 grams of water salted to 5 per cent.; this liquid, passed through a candle-filter sterilized in an autoclave, gave a residuum of 55 grams. This residual liquid was called nephrine, and 3.5 grams were injected per diem. These injections seemed somewhat painful, but do not appear to have caused any local trouble.

The glycerin extract used by us two years later was prepared as follows; it is this one that we have always employed in our hospital experiments, and afterward in private practice:

The kidney of a pig is carefully extracted in a sterilized vessel; in the laboratory this organ is cut into thin sections and set to macerate in pure glycerin at 30° C. At the end of 24 hours the glycerin marks 20° Baumé, which shows that it has extracted from the macerating kidney 30 per cent. of its juice, so that the glycerin extract is composed as follows:

Anhydrous glycerin,	67
Glycerin water,	3
Renal juice,	30

The extract, to which chloridized water is added to make the injections less painful, remains two hours in a d'Arsonval's sterilizing filter under 60 atmospheres pressure of carbonic acid gas, and is then filtered through a d'Arsonval porous candle at the same pressure. The liquid when filtered comes out perfectly limpid, and is enclosed in bulbs sealed by a blowpipe, each bulb containing per cubic centimeter all the soluble elements of 10 or of 25 centigrams of renal substance, according to whether the original glycerin extract was diluted in ten or in five parts of salted water. The dilution in five parts seems to be preferable for therapeutic use. Age appears to have little effect on extracts prepared in this manner; so long as the liquid remains limpid it is good for use.

Although this substance has been said not to contain the essential elements of glandular structure, to judge by the results given, we

do not think it possible to deny that these extracts have a real physiologic action. The two detailed cases we published appear to leave no uncertainty on this point. With the first patient, a woman of 54 years, who had suffered for five years from interstitial nephritis, complicated during the last two months with serious signs of auto-intoxication, headache, disordered sight, vomiting, edema, and, finally, an enormous decrease in the urinary toxicity estimated according to Bouchard's method and represented by a uro-toxic coefficient of 0.136 to 0.216,—this coefficient was seen on the second day of the opotherapeutic treatment to rise to 0.368, the urea and salts to undergo slight increase, and the phosphoric acid in particular to pass from 0.28 to 1.24 grams, while the quantity of albumin remained almost invariable. And at the same time that these important changes took place in the urinary secretion, the attenuation of the auto-intoxication signs advanced in such a rapid manner that, three months later, the albumin having practically disappeared, the patient was able to leave the hospital in a satisfactory condition. With the exception of a slight relapse a few hours later after overwork and errors in diet, the improvement in the case has been maintained, so that, after three years, in spite of a busy and sometimes fatiguing life, we found the patient in a good condition of health; nothing but the elevation of her arterial tension and the presence of a slight presystolic galloping rhythm betrayed the relative inferiority of her circulatory system and the lurking irritation of her kidneys.

The same favorable changes in the urinary secretion were observed in our second case, a young woman of 31 years, mother of 13 children, and suffering since her last confinement from serious tubercular nephritis: decrease in urinary toxicity (the average uro-toxic coefficient rising from 428 to 502), moderate increase in the amount of urea and chlorids eliminated, an almost doubled elimination of phosphates, and disappearance of the albumin. Still, as the patient was already in an advanced stage of tubercular cachexia, she finally succumbed to the progress of the infection that was undermining her, although the albumin did not reappear to any appreciable degree,—at any rate, without at any time manifesting signs of uremia.

Our experiments have been repeated with great care by M. Jacquet, as they have also been many times in our wards, and all

results agree: marked improvement in the uro-toxic coefficient and in the elimination of phosphoric acid, but only slight variation in urea and total nitrogen; in some cases slight increase in the oxidation coefficient, but very often continuation of the nitrogenous ratio previously observed; finally and chiefly, very marked steadiness in chlorid elimination. These points are worth bearing in mind; their interpretation will be given farther on. For the moment we will only observe that this urinary hypertoxicity is due to a special and direct action of the injected products, and is not the result of greater elimination of waste material caused by energetic combustion, which urologic analysis shows to be lacking. Furthermore, a series of inoculations made on animals with normal urine, combined with nephrine in much larger doses than are usually given to patients, proved that the elimination of the drug has nothing to do with this remarkable increase in the urinary toxicity.

The clinical results of subcutaneous injections of nephrine have confirmed on many occasions the hopes that our first experiments had awakened in our minds; we possess many case-histories in which the systematic use of the drug succeeded in relieving the most distressing symptoms of renal insufficiency: constant crises of dyspnea, rebellious uremic headache, and gastro-intestinal manifestations revealing most serious auto-intoxication. And in our opinion one of the best proofs of the usefulness of the method is the persistency with which, on more than one occasion, a hospital patient thus treated has asked for an injection, whereas, if we except morphin habitués, hypodermic treatments are not held in high favor among hospital patients.

Let me recall one more instance, a business man from the country, who came to see me about ten years ago for chronic nephritis with hypertension, enormous heart, enlarged liver, and edema reaching half-way up the thighs and threatening the large serous cavities. He hardly reached Lyons before he was seized with alarming signs of uremic dyspnea; he took to his bed, and for several days his condition grew worse so steadily that I feared a fatal ending in a very short time. I finally resorted to nephrine injections, and morning and evening two cubic centimeters of the 1 to 5 glycerin extract were given hypodermically. Relief was rapid; when the crisis was once passed, with a milk diet, together with cardiac diuretics, inhalations of oxygen, and other means, the improvement in three weeks

was such that the patient was allowed to return home. On several occasions relapses occurred, which were relieved each time by the same means, that is, by a series of 12 to 15 nephrine injections. But little by little improvement pointed toward a more settled condition, and now, ten years later, this man, still at the head of his business, manages his affairs and appears to have the usual attributes of health to those who do not know more about him.

I also obtained equally good results, though less lasting, in the case of a young woman with gastro-intestinal uremia tending toward coma, and who seemed to me affected with cystic renal degeneration. A number of therapeutic attempts had been made with no result, and her situation seemed to me very serious when I proposed the nephrine injections, 2 c.c. twice a day. The improvement obtained was so rapid and complete that the persons about her were astounded at her restoration. But the nephrine, which had been so successful against toxemic symptoms, had no action on the actual working of the kidneys, whose impermeability remained very marked, with a coefficient $\frac{\Delta}{\delta}$ of about two unities for a total molecular diuresis that did not reach 2000; so that, in spite of the very great improvement obtained, we remained on our guard, and expressed to the relatives our fear that the intoxication would appear once more. This happened only a few weeks later, and carried off the patient without our being able to do anything to save her.

Therefore, for our part, taking into consideration experimental facts and clinical observation, it seems difficult to deny that renal opotherapy, by means of injections of glycerin extract of renal pulp, has a manifest action on the accidents due to renal impermeability.

The question arises as to what has prevented the diffusion of a method of treatment that is easy to put in practice and costs little? Therapeutic scepticism? or frequent failure in presence of symptoms commonly so grave? The chief explanation is, in our opinion, that, as a rule, the nephrine has been tried only as a last resource, when the nephritis has reached the final phase in its evolution. But if we consider that the remedy cannot pretend to regenerate the parenchyma destroyed, that even, according to the minute analyses mentioned above, its introduction into the system has a hardly appreciable action on glandular function, and that consequently we can only have to deal here with some direct action on the tissues, whose resistance or inaptitude to retain poisons is increased by the

nephrine, or, possibly, with some direct action on these poisons themselves, they being transformed in their chemical constitution and thereby rendered easier to eliminate; consequently, it is evident that nephrine cannot be looked on as endowed with any curative power properly so-called. It is a means of temporarily neutralizing the ravages caused by retained toxic substances, until such a time as the kidney, having become more permeable, will allow them to pass through, or until other complementary organs shall have eliminated or destroyed them.

The good results of this treatment can only legitimately be looked for during the evolution of Bright's disease when there is uremia due to impermeability caused by temporary functional suppression of zones that had remained in a relatively healthy state by the side of glandular zones destroyed, and that were capable, consequently, of recovering, for the time being at least, their functions.

It is because this class of cases had not been sufficiently set apart, and because the method had been applied in too general a way, that failures occurred, which led many to think that the treatment lacked efficacy.

II

The idea of making up for the want of internal secretion by means of the injection of a certain amount of blood serum extracted from the renal vein is also an outcome of Brown-Séquard's conception, of which it is, as a matter of fact, the most rational application. It was only after the general discussion raised at the Montpellier meeting of the French Medical Congress in 1898, on the results of opotherapy that this idea took shape, and seemed to us susceptible of a practical application; though Bra had, in 1895, broached the subject by querying "whether the blood leaving an organ, and which contains, consequently, the products of internal secretion of that organ, would not act more usefully than an extract made from the entire organ." This idea had also been carried out by other experimenters in treating artificial uremia in the dog.

Starting from these experimental and clinical data, I undertook to give this new renal opotherapeutic method a systematic trial, in the hope of obtaining more energetic, and especially more rapid, therapeutic results, and of being in a position to be able, in case of necessity, to get the upper hand of an attack of fulminating uremia, in which the nephrine injections often fail. This expectation was not

ill-founded, and, after acquiring a sufficient supply of the renal venous serum of a goat, prepared with all desirable precautions of asepsis, in June, 1898, we were ready to use the method systematically and to observe its results with all the necessary accuracy. These first experiments were most encouraging; thus, we had the satisfaction of witnessing the practical resurrection of a boy of 15 years, with scarlatinous anuria, massive albuminuria, granular casts, intolerable headache, and tenacious vomiting, and apparently impending death, through an injection into the cellular tissue of the right side of 20 c.c. of this serum. The very evening of the injection the improvement was such that the battle was virtually won, and in five days' time the patient seemed entirely convalescent: headache and vomiting had ceased, casts had disappeared, and the urine, risen to three litres in 24 hours, was carrying off 18 to 20 grams of chlorids for the same period.

If we had only this one case to base the method on, it would behoove us to be modest, as the most pronounced cases of uremia can sometimes retrocede spontaneously, particularly when occurring in the course of acute nephritis, and especially in scarlatina. But other equally convincing cases can be cited. There is, for instance, Turbure's case, in which the action of the defibrinated renal venous blood was followed step by step: its influence on urinary secretion, the variations in albuminuria, the toxicity of urine, as also the evolution of the symptoms corresponding to these elements; in this case we were also able to convince ourselves of the efficacy of the treatment in a direction always the same, at each of the six different onsets of the renal intoxication. There are also two cases seen by de Lignerolles in which the action of the injection of renal venous serum appeared unquestionable. The first was a case of uremic dyspnea with acute edema of the lung and nephritic pericarditis; and improvement after four injections was such that in less than three weeks' time the patient, completely freed from his respiratory disorder, and having gained $2\frac{1}{2}$ pounds in weight, in spite of the disappearance of her edema, asked to leave the hospital, having only a few rhonchi at the bases of her lungs and a slight rubbing sound over the pericardium. She, therefore, went away, although warned that relapse might occur, as indeed happened, the patient returning in about a month's time, when she succumbed to a crisis of asystole that could not be overcome.

The immediate effects of the renal serumtherapy were equally conclusive in the second case, a woman of 62 years, with chronic nephritis and enlarged heart, manifest presystolic galloping sound, marked impermeability to methylene-blue, large quantity of albumin, and pronounced nervous symptoms, disordered speech, hemiparesis on the right side, etc. The second day after the first injection the improvement was striking, the albuminuria had become insignificant, and the nervous symptoms were so much better that the woman could speak correctly and could use her right hand well enough to carry a glass to her mouth, whereas previously she could not even hold a pencil.

Consequently, the good effects of renal serumtherapy, used under the conditions mentioned above, seem to be beyond criticism. The technic adopted is as follows:

Turbure used renal and venous blood of the dog after simple defibrination, thinking that the toxic principles contained in the circulating blood reside exclusively in the plasma; of this he injected 12 to 14 c.c. without, in his cases, the injections giving rise to any marked local reaction. I prefer to use serum extracted by aspiration from the renal vein of a goat, an animal that is usually refractory to tuberculosis, and whose serum is slightly toxic,—less than that of man. Of this I injected 20 c.c. at a dose under the skin of the abdomen. The injections were always well borne, although, after causing temporary rise of temperature, in some cases even severe,—the thermometer rising to 102° to 104° F. during the day following the injection. But, as it has been shown that serum loses its toxic action with age, without losing its anti-toxic properties, which it retains for many months after extraction, we feel that it is preferable not to use fresh serum.

The effects of the inoculation are rapid, as a rule. The symptomatic disorders—vomiting, dyspnea, stubborn headache, etc.—decrease in a few hours, in spite of the pyrexia to which we just referred, and which is often accompanied by loose bowels. At the same time important modifications in the composition of the urine appear: first, a decrease, sometimes remarkable, in the albuminuria; then, and this regularly, together with improved diuresis, marked increase in urea and chlorids, slight decrease in phosphates, and, in most cases, decrease, immediate at least, but very marked, in urinary toxicity.

This last point deserves close attention. We have considered it at length, without finding any satisfactory explanation of it; but it constantly appears in Turbure's analysis; it also occurs in almost all of the cases cited by de Lignerolles, and without possibility of confusion or of mistakes in interpretation. The figures are significant, as they point to wide differences. Turbure mentions a drop in toxicity from 264 to 162, and from 726 to 245. De Lignerolles, on his side, gives urotoxic coefficients falling from 340 to 132, 111 to 78, 310 to 132, etc. It is all the more important to call attention to these points in that they are not easy to interpret and appear paradoxical,—at any rate, contradictory,—when compared with what was said above concerning the effects of injections of nephrine, which manifest their influence, on the contrary, by increased urinary toxicity.

The reconciliation of these discrepancies is not easy, as we are obliged to remain on the ground of hypotheses; the necessary conclusion seems to be that the two methods, while affording analogous results, accomplish these results in ways that are certainly different. We saw that nephrine appears to have on the cells of the tubules, as well as on the glomerular circulation, an effect that is insignificant or nil; in the present instance the case is different. The active modification of renal function, showing itself in strong elimination of urea and chlorids, is also very probably accompanied by increase of the endo-secretory function of the epithelium, and consequently of its internal antitoxic value; it may also be that the antitoxins contained in the serum injected are susceptible of neutralizing to a certain degree the used material and waste products retained in the circulation; it may be, finally, that this serum, capable of inducing intense general reaction, sets up in the system phenomena of defence by stimulating, for instance, the functional activity of certain organs that destroy poisons, such as the liver, whose freer intervention agrees well with the excessive nitrogenous elimination noted. All of which conditions may have as a logical and necessary result the lessened toxicity of the blood in circulation, and ultimately that of the urine, a twofold situation that usually accompanies improvement in the symptoms.

The problem is, therefore, extremely complex, and we cannot pretend to solve it definitely in the present state of our knowledge. But what cannot be questioned are the results accomplished, and,

whatever may be the interpretation of them to be supplied in the future, they must already be looked on with great clinical interest.

III

The third method employed to make up for the functional insufficiency of the kidney consists in making direct use of the pulp of the raw organ, and in giving by the stomach a maceration of the entire gland. This might be called integral opotherapy. This method was advanced in Russia as far back as 1895, and applied to a certain number of patients; some French practitioners next resorted to it occasionally, when no glycerin extracts were at hand. But the method had not spread at all, and it was not until the well-known papers of Dubois and Renault appeared that the attention of the medical world was really directed to it.

Integral opotherapy has been carried out equally with the kidneys of sheep, pigs, and calves. One physician has gone so far as to administer daily the pulp of 20 to 30 sheep's kidneys. Dubois gave the maceration of three pigs' kidneys a day for two consecutive weeks. Renault also advises two or three pigs' kidneys per 24 hours, but only during ten days, to avoid signs of intolerance, which are not infrequent.

This is Renault's method given in full in the paper he read on the subject before the Academy: Remove the capsules of two or three pigs' kidneys, wash thoroughly, and cut up fine and mash in a mortar; to the pulp thus prepared add 450 grams of water salted to 7 per cent., macerate for four hours, then decant carefully. This liquid, about 3 to 4 teacupfuls, contains the greater part of the really useful glandular elements; all that is then required is to give it in a little milk or bouillon in three or four doses.

The patients generally show some repugnance at swallowing this preparation; but with perseverance it is not difficult to overcome this initial distaste, particularly as, in our opinion, it is not really necessary to resort to such concentrated macerations, a single pig's kidney having on several occasions appeared to us to realize the desired therapeutic effect, an advantage that is not to be despised, in view of the unquestionable toxicity of the maceration of organs.

But this effect cannot be doubted in a certain number of cases; without counting the examples on which Renault based his demonstration, we have knowledge of several instances in which improve-

ment in general conditions and toxemic symptoms clearly followed the administration of the glandular maceration, while at the same time the urine showed progressive decrease in the albuminuria.

Unfortunately, it is not always easy to resort to the method. Some patients cannot overcome their repugnance; with others the existence of serious gastro-intestinal disorder renders all administration by the stomach impossible; still others manifest signs of intolerance or of toxic conditions (urticaria, diarrhea, bullous eruptions, etc.) which make it necessary to abandon the treatment. I even know of a certain number of patients in whom the symptom albuminuria was made so much worse that the treatment had to be stopped. Possibly a more improved technic may free the method from these various drawbacks, which depend unquestionably on the presence in the liquid absorbed of toxic substances, elaborated or condensed in the glandular cells, and which sterilization of the product of maceration, or its filtration under pressure, might remove.

Unfortunately, the cases published by Renault are not explicit enough; the absence of exact information concerning the condition of the renal permeability before and after using the serumtherapy, the almost constant silence as to the rate of chlorid elimination, the lack of all examination as to cryoscopy or urinary toxicity, do not enable us to make a close comparison between this opotherapeutic method and the two that have gone before,—which would have been of the greatest interest. We can, therefore, only make partial comparisons; so far as they go, we are inclined to think that kidney maceration acts more like nephrine than like the serum of the renal vein, that is, in diminishing signs of toxemia, in acting directly on tissues or poisons, and in not modifying in any particular way the functions of the kidney itself. For the only complete analyses of which we are acquainted show relative steadiness in the elimination of chlorids and only unimportant differences in the cryoscopic values of the urine examined before and after the opotherapeutic treatment.

Renault ventured on a most ingenious explanation of the effects of integral serumtherapy, although it is still entirely hypothetical. He raises the point whether, through the product of renal maceration, we do not introduce into the circulation, to be subsequently taken up by the tubule cells in virtue of a species of elective property,

special organites called "secretion or segregation atoms," organites that play in the healthy epithelial cells the rôle of actual poison condensers. These organites, altered or destroyed in renal degeneration, and no longer bringing their special properties to bear on the toxic substances to be eliminated,—the poisons retained in the blood will be at liberty to exert their baneful influence until such a time as new secretion grains, artificially introduced, shall condense them again in the protoplasm, whose work it is to attend to their elimination.

This idea, it is true, is based on histologic facts that have been proved. The existence of segregating atoms cannot be questioned; the work of Heidenhain, Tridonneau, and Gurwitz has settled this point, and the quite recent research of Renaut on the structure of the kidney of the snake have clearly demonstrated these vacuolar atoms accumulated in the supernuclear region of the epithelium, while at the same time it has shown with entire precision the different aspects of their evolution under the influence of various stains. Again, all competent naturalists adhere to the doctrines of Overton and Gurwitz, and are of opinion that substances intended to enter into the renal cells pass through their wall either through the help of the lipoid elements for the so-called vital substances, or through simple osmosis for dissolved substances, and condense themselves afterward in the protoplasm of the cells, the former in the infranuclear zone in the shape of lipoid vacuoles, the others in the form of segregating atoms between the nucleus and plateau of the cell. The quite recent researches of MM. Renaut and Policard, while differing on some secondary points, have only confirmed the importance of these doctrines.

It is easy, then, to understand that a distinguished histologist like Professor Renaut should be seduced by facts so well established, and should be tempted to apply to clinical medicine the data furnished by a conception so strongly backed up by trustworthy research. But we must admit that such theories cannot be applied to human pathology without reserve. To begin with, the segregating atoms, although probably extant also in the kidney of man, have not yet been demonstrated there. It does not seem, either, that M. Renaut has even isolated, in the product of renal maceration prepared for ingestion, these atoms supposed to condense poisons; and, even admitting that a property analogous to that which, according to

Metchnikoff's conception, collects the nephrolysins in the renal elements to the exclusion of all other parenchymata, attracts in such instances in the diseased kidneys the atoms administered and having reached the circulation intact, it would still be difficult to understand how histologic elements representing structured organites would be capable of passing through, without previous modification, the membranes of damaged cells whose protoplasm has become unsuitable to retain similar elements.

Wherever the truth may lie in this discussion, made imperative owing to the notoriety of its principal defender and to the favor with which were received the first clinical results published, it nevertheless remains certain that in some cases the ingestion of a maceration of pigs' kidney has overcome the symptoms of renal insufficiency and reduced correlatively the degree of the albuminuria. The method should, therefore, be used in practice, provided it is applied with prudence and discernment, that the dose of macerated parenchyma is diminished, and that the fact should not be lost sight of that macerations of organs have toxic properties which make it necessary to use them with every precaution.

IV

Nothing now remains save to determine the clinical indications to be filled by renal opotherapy, and the rules that are to guide us in choosing the preparation to be used. In a general way, opotherapy appears to us to find its application in all cases of renal insufficiency of whatever importance, acuity, or significance. But, as has already been remarked above, we are not warranted in counting on really useful effects unless the parenchyma is not too seriously disorganized and the case is rather one of uremia due to sudden interruption of renal activity (acute nephritis, intense congestion of the kidneys producing temporary oliguria, calculous anuria, etc.), or to functional suppression in a kidney previously diseased of portions of the parenchyma that had up to that time remained permeable, but that were thrown for the time being out of order through sudden strain or the action of intense cold, as in attacks of temporary uremia due to congestion in a polycystic kidney, or in one stricken from the start with interstitial nephritis). It is easy to see that in such circumstances opotherapy may be of real service in counterbalancing the toxic effect of retention products until such a time as the treatment

employed (general or local blood-letting, revulsion, diuretics, etc.) shall have again opened the channels of excretion, reëstablishing in the permeability of the gland the relative equilibrium that has been upset by the disorder present.

In this way renal opotherapy serum was particularly an excellent temporizing means, that will give the rational treatment of the disorder time to act, a means, in a word, that can be resorted to when the kidney falls short of its duty, just as digitalis is used during a crisis of cardiac insufficiency, but which is no more capable of repairing the anatomic damage present in the kidneys in Bright's disease than digitalis is capable of repairing the lesions in the myocardium or in the valves.

It is unquestionable, according to our personal experience, that hypodermic injections of renal vein serum are the most active and efficacious methods. It is to them that we prefer to resort in fulminant cases threatening life, where the main point is to do something quickly. The objection will no doubt be made that the method is not easy to apply, and that renal venous serum cannot be got at any moment. This is not an insurmountable difficulty, given the number of serumtherapeutic laboratories now established and the length of time during which the antitoxic properties are retained by this serum once prepared. But if no serum can be had, injections of nephrine should at once be made (2 c.c. morning and evening, if there is urgency), or the direct maceration of kidney tissue should be prescribed, provided the condition of the patient's digestion permit. For, even though the case seems a desperate one, the antitoxic effect of the glycerin extract has always, in part at any rate, a moderating action on the most distressing symptoms of uremia, and specially on headache, vomiting, and attacks of dyspnea; in fact, in some cases the satisfaction will be experienced of seeing all the symptoms disappear and the patient regain health. These fortunate cases are not rare, and many physicians have reported such occurrences. This manifold testimony appears to me sufficient to prove that between the results obtained and the treatment employed there is a necessary relation, and that the favorable outcome in these instances is not to be attributed to fallacious coincidences.

Remembering, again, that extensive epithelial lesions are always accompanied by general decrease of strength, cardiac asthenia, and marked signs of anemia, we are strongly tempted to think that the

internal secretion has not only an antitoxic effect, but possesses as well an excrementitial influence, and that it acts on the rate of interchange, and perhaps also on the fermentative process, of intracellular life,—whence the legitimate inference that opotherapeutic extracts may and ought to find their rational application in offsetting in weakened cases of Bright's disease the deficit in the endo-secretory process. We think, consequently, that it will be found useful during the evolution of epithelial nephritis to recommend from time to time, and for regular periods, an opotherapeutic treatment, even when there are no uremic complications. Thus in many cases we have advised (for 12 to 15 consecutive days every two months) a daily injection of 1 c.c. of nephrine as a tonic or restorative remedy. On the same basis we have, with certain patients, thought it desirable to substitute in the place of nephrine injections (our supply having run short), injections of testicular liquid, or, oftener still, with patients opposed to hypodermic treatments, Poehl's solution, prepared for administration by the mouth, in doses of ten drops twice a day in a little Vichy water; the results obtained have been very similar; we have then noted improvement in strength, increase in arterial pressure, and sometimes noticeable decrease in the amount of albuminuria. This effect of testicular opotherapy applied to the treatment of Bright's disease is interesting, as it throws a certain amount of light on the rôle of internal secretions and on the way in which they influence the intimate phenomena of nutrition.

In general terms, patients with mixed or parenchymatous nephritis, in whom the test of phloridzin glycosuria is negative, are those that appear to us particularly suitable for the systematic and prolonged application of renal opotherapy.

In conclusion, renal opotherapy, in whatever form it may be applied, is a therapeutic method that physicians will do well to use. Provided it is judged in its true light,—that curative results are not expected from the method, but that it is looked on as a sometimes powerful, and almost always useful, coadjutor of the means usually employed in overcoming the symptoms of renal insufficiency, whatever may be their kind,—physicians will find in its use other results besides disappointment. As for the process to be employed, it must depend on the exigencies of the situation, on the intensity and suddenness of the attack, as well as on the patient's individual tolerance.

SERUMTHERAPY

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Of New York City

WITHIN the last few years there have been placed upon the market medicinal products which, when injected into a body infected with certain diseases, have the property of strengthening the natural resources to combat conditions arising from the disease. These products are called "antitoxins" or "serums," and their use the "serum treatment."

In their preparation the natural processes that take place inside the human body in its fight to overcome infection and its effects are duplicated outside the human body,—that is, in the serum of animals. An "antitoxin," therefore, is a modified serum (properly purified) which has the property of assisting in combating infectious diseases and their effects in the same manner as that possessed by the human body itself.

Antitoxins or antibodies are specific substances that measurably exist in the human body and are formed in the animal body, particularly in the blood serum, while the body is passing through and has recovered from a disease caused by the influence of a specific infection. The perception of the existence of these substances in the blood serum, as well as the knowledge of their quantitative increase commensurate with the quantity of the poison introduced into the body of a thus protected animal, is the foundation of our present serumtherapy. Serumtherapy is, therefore, the practice of introducing into the body a sufficient quantity of antitoxin to destroy certain poisons, which have been received into the body by infection, or have been produced in the body by some specific excitant. The serum taken from an animal thus protected against the poison of a specific bacteria can serve to protect another animal or person usually *only* against the poison of the same species of bacteria.

The benefits which have been reported to attend the use of specific serums in uncorresponding diseases may be due to the

alexins which are found in all serum, but are not thought to be due to any specific element in this particular serum which is absent in normal serum.

In the consideration of serumtherapy it will be necessary to touch lightly upon the influence of predisposition and immunity to disease, the chemical toxic products of microbe life and their influence on the living organism.

There is no fact in clinical medicine more clearly established than that the human body has within it natural resources for combating disease processes and effects. But these resources have their limitations in the same individual at a given time, and in different individuals at different times, while these become progressively weaker after the limit has been reached and passed. The inadequacy in some cases of the natural resources to combat successfully disease conditions is well known, but it is particularly obvious in certain infectious diseases, such as diphtheria, smallpox, tetanus, septicemia, etc., in which the bacteria causing the disease multiply with almost unmeasurable rapidity, and the decomposition products (toxins) are so large in quantity and so virulent in character that they tax the system to its utmost to eliminate them, or, this failing, they quickly cause death.

There is but one short step between the causes of the phenomenon called wound infection, with its correlative systemic manifestations, and those of systemic infections from other sources. This step is nearing its completion, especially since our biologists have succeeded in their investigations concerning the causes of malaria. The sources of tuberculosis, tetanus, hydrophobia, diphtheria, variola, etc., etc., are quite established. But the question how therapeutically to counteract and prevent the invasion of these microorganisms is one of the greatest moment. No one who is well informed on the subject doubts the herculean nature of the task, nor denies the boon it may bring to humanity. It seems almost incredible that, while a century ago vaccination solved the problem of how to control variola, yet at this date we have accomplished so little in the field of serumtherapy. The diphtheria antitoxin has the lead in this field of study, while in tetanus, hydrophobia, and perhaps plague, we have given the full list of infectious diseases in which we may look for good achievements with considerable hope in the immediate future. At present the biologist is confronted

with a dual aspect in the labor. This consists of the antitoxic serum on the one hand and the specific bactericidal serum on the other.

The antitoxins—typically observed in diphtheria—have proved more successful than the bactericides, and differ in their action, as their name indicates, in that they do not act upon the infecting bacterium directly, but counteract the toxic product thereof, perhaps by uniting with the toxin, thus protecting the endangered cell, not by destroying the disease germ itself; while the specific bactericidal serum, on the contrary, destroys the life of the bacterium, but has no effect upon the toxin. The former, which act upon the toxin, merit quite an enviable as well as leading position in the list of therapeutic agents. The latter, by far the longer list, have been of less practical utility to date. Behring, Pasteur, Koch, Pfeiffer, Calmette, Metchnikoff, Ransom, Roux, Wassermann, and others have labored incessantly in this most important field of research. One will see here *the* opportunity for scientific revelation in comparison with which all past scientific achievements dwindle into insignificance. Much as antisepsis has done for humanity through surgery, a hundredfold more good would follow the inauguration of effective immunizing and specific bactericidal sera.

While the progress along this line seems slow, and while those unfamiliar with the enormity of the task become suspicious and skeptical, it can be truthfully said that the hope for ultimate success never was brighter. That which twenty years ago was in a state of chaos has already assumed form and system. Hypotheses have become established facts. Theories that were the objects of research and quest have become the basis of new experiments, and, if we were forced to choose between the two: whether or not the infectious diseases sooner or later would have to yield in their ravages, as did variola a century ago, we would unhesitatingly answer yes.

Davaine first demonstrated that the blood of an animal suffering from anthrax, when injected into another animal, reproduced the disease, while the same blood, carefully filtered so that all anthrax bacilli were eliminated, became innocuous. Pasteur later found that when the bacilli of anthrax or chicken-cholera were cultivated in bouillon at a relatively high temperature, they lost part of their virulence. He found, further, that animals inoculated with these "attenuated" cultures gradually became immune to the most viru-

lent form of the corresponding disease. This procedure has gained wide practical application in protecting animals against anthrax and chicken-cholera in infected localities. It was at first supposed that the various bacteria, related to the infectious diseases, were the cause, not only of the disease, but also of the symptoms coincident with the disease. More accurate observations, however, have proved that the manifestations of the various infectious diseases are in most instances caused by the chemical poisons of serum-culture toxins produced by the microorganisms in their growth. Diphtheria gives us a very rational example of this. We have here a disease in which the microorganism rarely extends beyond the superficial tissues of a limited area of the throat, only at times penetrating the mucous membrane to the submucous tissues. Death in diphtheria is usually caused by nerve-degeneration—be it of the cardiac ganglia, the vagus, or the nerve-centers. These degenerations could not possibly be caused by the microorganisms themselves, as they are not to be found except at the seat of the local lesion, but are caused by the toxins generated by the microorganism in its life-growth and taken into the circulation.

Briegee was the first to succeed in isolating some of these toxins, or tox-albumins, in an almost pure state. Further experiments proved that animals gradually inoculated with the toxins obtained from cultures were rendered more or less immune to the specific disease, such as, for instance, diphtheria, tetanus, septicemia, cholera, glanders, etc.

As to the origin of antitoxins, there are two leading theories: the chemical, and the biologic or cellular. The chemical theory supposes that the antitoxin is produced in the body by certain chemical changes due to the presence of toxins; the biologic theory considers antitoxin as a product of certain body cells. Different antitoxins will be formed by the action of different toxins, and the amount will be in proportion to the length of time during which the stimulus acts or in proportion to its force, not to its quantity. Among animals it is observed that certain ones, particularly of the cold-blooded type, do not form antitoxin; for example, an alligator may be injected with enormous doses of the strongest diphtheria toxin, and no antitoxin will be formed. Such facts prove that a toxin undergoes no chemical change in the blood of an animal endowed with a natural immunity.

Concerning the habitat of the microorganisms of disease, we now know that it is found in the beginning stage not so much in the blood as is usually believed, but in the serum of the cellular tissue.

As has been indicated, the question of how immunity is produced and what is the nature of this immunity, has been variously answered. One is that it is due to the direct bactericidal action of the fluid. Another (Metchnikoff) that resistance is gained through the phagocytic action of the polynuclear leukocytes especially, whereby the causative microorganisms (as can actually be observed on the warm stage under the microscope) are absorbed or digested by the phagocytes. Ehrlich believes that the action of antitoxin depends upon its chemical combination with toxins resembling the action of an acid when brought into contact with a base; but the probability is that immunity is the complex sum of various factors: the germicidal action of the blood serum and tissue fluids, the phagocytic action of the leukocytes, and the antitoxic action of the alexins.

The tissue-cells or the leukocytes, or both, when microörganismic infection occurs, form certain new substances designated alexins, which have the peculiar power of neutralizing the toxin produced by the microörganism. These alexins or antitoxins are, in fact, produced, whether the attenuated cultures or their toxins are injected, and gradual immunity to even virulent and enormous doses is produced. The blood serum of animals thus gradually immunized, if used for the inoculation of healthy animals, will render them insusceptible to the poison, or, in other words, act as an antitoxin. This immunity against infection is, however, more or less transient, and is, as we know, both clinically and bacteriologically considerably influenced by various factors, such as cold and exposure, inanition, etc., which depress the vitality and predispose to infection and disease.

Immunity may be considered under three heads: Natural, or that which certain races or species of animals possess at all times against certain diseases; inherited, or that which is transmitted from mother to child through the placental circulation or through the milk; acquired, or that which is produced by one attack of the disease, through vaccination, or by treatments with cultures, either sterilized or unsterilized, of the specific microörganism. Acquired immunity may be active or passive. By the former is meant the immunity produced by the direct treatment with cultures so that

the antitoxic or antibacterial substance is produced in the body of the animal treated. By passive immunity is meant that produced by injecting the serum of an actively immunized animal into a second animal.

As has been said, the conditions which secure immunity are varied and numerous. For example, before pathogenic bacteria can be productive of harm, they must secure a suitable port of entry, some of the most poisonous being entirely harmless when injected into the body subcutaneously, but rapidly fatal when taken into the alimentary canal. This is the case with the vibrio of Asiatic cholera. The very opposite, however, obtains with the bacilli of tetanus and anthrax. After finding an entrance into the body there are many obstacles to overcome before the microörganism can proliferate and become harmful. It may be destroyed by the gastric juice, or it may be hurried out of the body in the secretions. Some micro-organisms do not seem of themselves to be harmful but through their toxins only. Then there is both bacterial and toxin immunity, for in some cases animals are insusceptible to the toxins, but easily affected by the microörganisms. Again, natural immunity consists in: Inability on the part of the microörganism to multiply in the animal body; the destructive action of the phagocytes on the invading organism; and plasmolysis, or the destruction of the invading organism on account of the new medium in which it finds itself placed. Acquired immunity is secured by treatment with attenuated cultures of the germ of the disease; by the employment of sterilized cultures of the specific microörganism, or by the use of its toxins; and by treating the animal with cultures of the specific microörganism mixed with the other bacteria, or by the employment of mixed cultures, in which the specific microörganism is present.

In the artificial production of the various antitoxins, animals, such as the goat, cow, or horse, for instance, are gradually rendered immune to the specific microörganism by the injection of either attenuated cultures rendered comparatively harmless by heat and cultivation at relatively high temperature, or very minute quantities of the virulent organism itself. The specific toxin—the chemical product of microbic life—is obtained either by the sterilization of the bouillon culture of the organism by heat (about 58° C.), the addition of 0.5 per cent. phenol (carbolic acid), or by filtration through a porcelain filter. After the animal has received gradually

increasing doses of the toxin, it is found to be immune to infection from the organism in question. Part of its blood is now withdrawn under strict aseptic precautions, and the blood serum constitutes the antitoxin.

DIPHTHERIA

The general conclusions regarding the average reduction in mortality from diphtheria after the antitoxin treatment by not less than 50 per cent., and under more favorable conditions a reduction to one-fourth or even much less of the previous death-rate, are drawn from more than 100,000 cases, collected from different countries and in different years, leaves no alternative but to accept its curative and immunizing properties as established facts. No doubt can exist to any one with average intelligence as to its reliability if employed early enough. It has been found that 200 to 300 units of diphtheria antitoxin will provide immunity against diphtheria for from 2 to 4 weeks, and these immunizing doses have practically entirely stamped out the disease from the large infant asylums, where it formerly was so destructive.

Diphtheria antitoxin probably acts in the human body by chemically destroying the poisonous products of the bacteria causing the infection. It exhibits also a physiologic action, supplying to the body the same elements that the body develops to protect itself against the poisonous bacterial invasion; but the true nature of the active principle of the diphtheria antitoxin is an unsolved problem. It may be an organic substance, an organized product, or an enzyme or soluble ferment (which are proteid or nucleo-proteid in character). The small dose of antitoxin, its rapidity of action, and its profound influence upon the human system, would suggest that it might be enzymic in character, although there is no positive evidence to sustain this theory. The power of some enzymes for work is almost unlimited. A sample of invertase which had inverted 100,000 times its own weight of cane sugar was found by O'Sullivan and Thompson to be still active.

The method of preparing antitoxins is of interest. That of diphtheria is typical of the others, and is as follows: A culture of diphtheria bacilli is grown upon Löffler's solidified blood serum, and the colonies grown are transplanted into faintly alkaline bouillon (in flasks) and kept at a uniform temperature of 37° C. The bacilli rapidly multiply and produce large quantities of a highly

poisonous product, toxin (diphtheria toxin), after which the bacilli are destroyed by the addition of 1 per cent. phenol (carbolic acid) or trikresol, and their dead bodies removed by filtration. The toxicity of the toxin, or rather its antagonism to antitoxin, is found by injecting it into guinea-pigs, the standard of strength being such that 0.01 to 0.1 c.c. should kill the control animal in from 24 to 36 hours. The antitoxin is then prepared by injecting the toxin into horses, which are used because they are most easily handled, and because they yield large quantities of a serum that is less irritating in its effects upon the human system than that of other animals. Further, horses are naturally immune to diphtheria, and this immunity is greatly strengthened by the toxin treatment. Disease-free animals only are employed, the mallein test being used to detect glanders, and the tuberculin test for tuberculosis.

The first injection of the toxin is usually 1 c.c., and this is repeated every 5 to 8 days in gradually increasing amounts. The limit of toleration is generally reached in from 9 to 12 weeks, when as much as 300 c.c. may be borne. As soon as the injection of large amounts of toxin causes but a slight rise of temperature, trial bleedings are made, and the product is tested. If the test proves satisfactory the horse is bled quite freely, the blood being collected in sterile bottles and cooled for a day. Each bleeding gives about 3000 c.c. of serum, which contains 300 to 400 units per c.c. The serum is then removed from the coagulum with a pipette, and preserved by the addition of phenol (carbolic acid) or trikresol. Finally the serum is standardized. The standardization is expressed in immunizing units. An immunizing unit is ten times the quantity of serum that is necessary to save from death a 300-gram guinea-pig that has received ten times its minimum fatal dose of toxin (determined by a series of experiments upon average animals per gram of body weight). This test is very accurate. When, for example, 9 units of antitoxin have failed to save the life of a guinea-pig, 10 units of the same antitoxin have saved the life of an animal of the same family, weight, etc.

This finished antitoxin is now placed in glass bottles or tubes, which should contain a fixed number of units to each c.c., ranging from 250 to 3500 units, and the glass containers hermetically sealed. The antitoxin retains its strength for six months or longer. The phenol (carbolic acid) or trikresol present makes the serum slightly

fluorescent in appearance, but does not precipitate the active principle or principles.

The old definition of the antitoxin unit—namely, that amount of antitoxin which when inoculated into a guinea-pig weighing 300 grams will neutralize 100 times the minimum fatal dose of toxin of standard strength, has been modified by Ehrlich, for he discovered that the toxin and antitoxin may vary greatly in strength. In order to secure a standard strength of both toxin and antitoxin for the purposes of tests, he prepares both of them in a dry, powder form and keeps them in vacuum tubes at a low temperature, protected from light. He mixed both the toxin and antitoxin before the injection, and uses the whole unit instead of $\frac{1}{10}$, and, instead of aiming for complete neutralization, he makes the death or the survival of the animal used the end reaction. He has discovered that there are present in toxins different degrees of toxicity as well as neutralizing power toward antitoxins. Animals are apparently more susceptible in winter than in summer.

The immunizing dose of diphtheria antitoxin is from 300 to 500 units. The dose as a curative agent should be from 1000 to 3000 units, according to the severity of the disease and the age of the patient. This dose is to be repeated in 12 to 18 hours if no improvement is noted and the case remains severe. Enormous doses in some cases have been shown to be perfectly harmless. Serum has also been used with the happiest results in cases in which the bacillus was localized in parts of the body other than the throat; for example, the conjunctiva.

McCollom, after a brief statistical resumé of the decrease in the general mortality in all cases of diphtheria following the introduction of the antitoxin treatment, calls attention to what may be accomplished in even the apparently hopeless cases by sufficiently large and frequently repeated doses of antitoxin. He says no hard and fast rule can be made regarding the use of the serum; it must be given until the characteristic effect is produced on the diphtheritic membrane; in some cases 4000 units will accomplish this result, in other instances 60,000 or even 70,000 units may be required.

As illustrating what can be accomplished in the face of a threatening fatality, McCollom gives in outline the histories of 11 patients, several of whom were almost moribund on admission; and the results obtained cannot fail to inspire with new courage those who

have been satisfied when they had given a paltry 3000 units, and should, moreover, persuade the doubtful and convince the ignorant. The amount of antitoxin employed in the cases cited varied from 56,000 units in a boy of 6 years, to 92,000 units in an adult, aged 34 years. All recovered, and in no one of these cases were there any serious complications as the result of the large doses of antitoxin, though in two instances an annoying urticaria followed. The conclusion is forced upon one that, in each instance, had not the antitoxin been given in large doses the result would have been fatal.

So long as there has been no septic change in the preparation (and this can be absolutely prevented), there need be no fear of overdosing.

Wonderful as has been the reduction of the mortality of diphtheria with the antitoxin treatment, it would have been still more pronounced had the fact been earlier recognized that the time to give the antitoxin is as early as possible in the infection, before large quantities of the toxins have been formed, and that the dose should be as large as the exigencies of each particular patient will permit. It also is better by far to give a larger dose than is apparently necessary than to err in the direction of too small a dose. When ferric hydrate is given as an antidote in arsenical poisoning, no one would think of giving just enough of it to neutralize the amount of arsenic actually taken; an excess is always employed to make the assurance of antidoting doubly sure. Similarly, when it is desired to arrest the effects of rapidly multiplying bacteria, an excess of antitoxin should always be used, and, if necessary, repeated in from 6 to 8 hours.

It is better to give an injection of antitoxin at once when diphtheria is suspected or probable rather than to await bacteriologic confirmation of the diagnosis.

Diphtheria antitoxin should not be kept upon the upper shelves of the store, where there may be excessive heat or gaseous fumes, but in a cool place, protected from light and dust.

TETANUS

Since the bacilli of tetanus remain at the seat of the infection and increase but slightly in numbers, the disease itself is a true toxemia, and not a septicemia. Its antitoxin ought, consequently, to be quite ideal, and such has repeatedly and everywhere proved

the case when it is employed as a prophylactic or immunizing agent before tetanic symptoms have appeared. In fact, the power of the tetanic serum to neutralize the poison before it has affected the cells is marvellous. After the injury to the cells its use is, however, not so satisfactory. Good results have, however, been obtained in cases after tetanic symptoms have developed, and an active, fresh antitoxin should certainly always be tried. Kitasato and Behring were the first to achieve success in rendering animals immune to tetanus, the immunity being against the toxins, and not against the bacilli themselves. The methods of administering tetanus antitoxin are the subcutaneous, the intravenous, and the intracerebral. Roux introduced the latter method. The underlying theory of Roux's procedure is that the nerve-cells have greater affinity for the toxin of tetanus than they have for its antitoxin. Consequently, by the subcutaneous or intravenous method, the toxins circulating in the blood may be neutralized, but not so with that in the nerve-cells. The chief difficulty in the successful treatment of tetanus by antitoxin is that the symptoms of tetanus do not develop until after a large amount of the toxins have been produced and absorbed, thus greatly involving the nerve-centers. The antitoxin cannot restore the nerve-cell to its normal condition. Therefore, it should always be used at once as a prophylactic when there is danger of tetanus symptoms following an injury. When so used it is a remarkable prophylactic. Ritchie has reported some interesting artificial modifications of toxins with reference to immunity. He has found that tetanus toxin is deprived of its great toxicity by treatment with hydrochloric acid, although its immunizing properties remain unaffected. It also loses its toxicity from the action of alkalis, such as sodium hydrate and sodium bicarbonate.

The initial symptoms of tetanus, as we see them, do not herald the beginning of the disease, but really the beginning of death from the disease. If possible, treatment should anticipate the manifestations of the nervous symptoms of the disease. For this purpose the injection of antitetanic serum as a prophylactic seems advisable in cases in which there is good reason to fear that infection with tetanus bacilli may have taken place. Tetanus serum is now made of such high antitoxic value that the injection of 2 or 3 c.c. would be sufficient, in the presence of a suspicious wound, absolutely to guarantee immunity from the disease. The mortality from tetanus

is so high that prophylactic injections are justified in all cases of burns or wounds where tetanus might follow. Intracerebral injections of antitetanic serum have not given the good results expected. Those who have used this method most, however, praise it, and continue to so use it in severe cases. Recently several cases of developed tetanus have been successfully treated by injecting the serum through a lumbar puncture. When so used it finds its way into the subarachnoid space, and very probably also into the ventricles of the brain, quite as effectually as if injected intracerebrally. Besides this, a certain amount of the toxins of the disease known to exist in the cerebrospinal fluid are evacuated, thus affording a large measure of relief. This method of injection after lumbar puncture is much simpler than the intracerebral injection, for, while the latter is a major operation requiring the skill of the surgeon and a complicated technic, the former is so simple that it can be done by any physician and at a moment's notice.

Exceeding care is required in making sure that the instruments, the solution, and the site of puncture are thoroughly aseptic.

Before leaving this subject I wish to reiterate my advice concerning the inadvisability of cauterizing these wounds. The effect is to coagulate the albuminous products of the tissue serums, thus effectively preventing the access of oxygen to the deeper tissues. Instead of cauterizing such a wound with the actual cautery or cauterizing with chemicals or strong antiseptics, it should be freely laid open to facilitate the free access of the oxygen of the air, which is the most effective germicide to the bacillus of tetanus, as well as the germ which causes rabies. Besides, counterirritants, when so applied if but a short time after the injury, do not affect the toxins and materially interfere with the comfort of the patient and retard the healing of the wound.

PNEUMONIA

The sudden fall in temperature and consequent amelioration of all the symptoms at the time of crisis in pneumonia has by many been considered as due to the development of an antitoxin in the blood. This seems, however, very doubtful, and many other factors bearing on the time of crisis may be pointed out, as, for example, that the majority of pneumococci in cultures die in about 5 to 7 days. An increase of acidity in the lung may also be

sufficient to prohibit the growth of the pneumococci, or the development of their toxin. The exudate of pneumonia, though within the lung, is practically outside the body, as far as the tissues themselves are concerned. It is in this exudate that the pneumococci flourish, and from this the surrounding blood-vessels absorb the toxic products.

Lambert, of New York, who, with Eyre and Washburn, in England, and Pane, in Italy, has worked most faithfully on this subject, and has come to the conclusion that even though the antipneumococcic pneumonia serum seems to prevent general pneumococcic septicemia, still it does not shorten the duration of the disease, nor bring about crises.

Dr. Brice W. Goldsborough,¹ reports 9 cases of bronchopneumonia and lobar pneumonia treated by him with antipneumotoxin with but two deaths. These cases were in patients varying from 6 months to 62 years of age, and all received alike 20 c.c. of the serum, repeated in eight hours, if the condition did not indicate improvement. In one case, an infant of 6 months, the pneumonia was complicated with diphtheria, with temperature of 105°, pulse 150, respiration 50. Two thousand units of diphtheria antitoxin were injected, followed in three hours with 20 c.c. of pneumonia antitoxin. There was gradual improvement of all the symptoms, though the injection of diphtheria antitoxin was repeated three times. The patient recovered in two weeks, without other treatment than stimulants and cold-water baths (to reduce temperature).

Of the fatal cases, one was in a child of 5 years, with bronchopneumonia following an attack of measles. When first seen by the author, the patient was in a deep stupor, with a temperature of 105°, pulse 150, and respiration 50, and in a state of extreme prostration. Twenty c.c. of the pneumonia antitoxin was injected, and this was followed by marked improvement in eight hours, the temperature and pulse being lowered with a return of consciousness. The attending physician and family refused further use of the serum, and the patient died in five days.

The other fatal case was in a patient aged 62 years, suffering from an osteosarcoma of the tibia. Amputation at the thigh was found necessary, after which pneumonia developed in the lower

¹ Jour. Amer. Med. Assoc., June 28, 1902.

lobes of both lungs. Then injections of the serum, 20 c.c. each, were administered at intervals of eight hours, with slight improvement, but the patient died. This was believed to be a case of metastasis.

Dr. Goldsborough tabulates 447 cases of pneumonia, some treated with the pneumonia antitoxin serum, some with the blood from convalescents, and 61 with antidiphtheritic serum. Of 386 patients treated with the antipneumococcic serum there was a mortality of but 16.5 per cent. Osler's tabulation of deaths from pneumonia in various hospitals in America shows a mortality of 25 to 35 per cent.

STREPTOCOCCIC INFECTIONS

Not only septicemia, but erysipelas, tonsillitis, cellulitis, bronchopneumonia, arthritis, etc., are caused by streptococci, of variable virulence, that occur alone or are associated with other germs. Besides these, many of the worst symptoms of phthisis, and certain conditions of diphtheria, are the result of streptococcic infection. We have, therefore, a wide field for experimentation in this line. It seems, however, that in none of these various streptococcic infections is there any striking tendency toward the production of immunizing or curative substances in the blood. The value of an antistreptococcic serum is very hard to estimate, and the results have so far in most instances been unsatisfactory and unsuccessful. Marmorek claims to have had positively curative effects in a number of cases of various kinds, and many reports of failures, as well as some successes, have appeared in the medical press. As the repeated injection of this serum certainly is lacking in danger, and as many cases of puerperal fever and septicemia undoubtedly seem to have been benefited by the employment of a freshly drawn and properly tested serum, it seems our duty to await further trials and experiments by careful observers before attempting to pass judgment on the subject. The recent reports from English workers would lead us to think that we have either not differentiated our varieties of streptococcus, or that we have not clearly defined our clinical varieties of septicemia. In regard to antistreptococcic serum, it has been discovered by Bokenham and Denys that the best product is obtained by immunizing the animals against as many kinds of streptococci as possible. By this method far more active serums are produced than can be obtained in any other way.

The treatment of *sarcoma* with the toxins of *erysipelas* and *prodigiosus* in the form of a watery extract, generally classed as a serum, as first recommended by Fehleisen, and largely carried out in this country under the directions of Coley, has in most instances met with failure, or but temporary benefit. As, however, the treatment is especially recommended in inoperative and progressive cases, and as in some such cases undoubted arrest or disappearance of the growth has occurred, the treatment certainly deserves further trial.

Since coccal serum produces only a very short immunity, and in some cases even an apparent predisposition, the same results cannot be looked for in its use as in that of bacillary antitoxins, which produce extended and even permanent immunity.

TYPHOID FEVER, CHOLERA, AND HYDROPHOBIA

Typhoid fever, cholera, and hydrophobia are some of the diseases that have also been treated with various kinds of serum, and, it may be added, with varying success. Much more thorough investigations will, however, have to be made before any decided views on the subject can be formulated for or against the employment of such serums. As to typhoid fever, Wright's method of treating it is to incubate a virulent typhoid culture for two weeks at 37° C., after which it is raised to about 60° C., until it becomes sterile. To this 0.5 per cent. lysol is added. A clear, sterile fluid is obtained by decanting, which contains the toxins elaborated by the bacteria, as well as the soluble fragments of the bacteria. Reaction takes place in 12 to 18 hours after injection. If the serum of an inoculated individual and that of an individual who has had the disease are compared, the former will have far greater agglutinating power than the latter. The serum of an inoculated individual should be examined a week afterward, and the clumping must occur quickly with a dilution of 1 to 50 before the inoculation can be considered satisfactory. Wright's reports are encouraging, since "they show that the proportion, on the one hand, of attacks, and on the other hand, of deaths, from typhoid fever was seven times smaller in the inoculated than in the uninoculated." Welch believes that there is sufficient experimental proof to justify the employment of the vaccine as a prophylactic measure against infection by typhoid.

A very valuable report has been made by Stokes and Fulton on serumtherapy in typhoid fever. They have made many animal ex-

periments, and sum them up as follows: "The subcutaneous injection of the serum in doses of from 1 to 600 to 1 to 800 of the body weight will protect guinea-pigs against four times the minimum fatal dose of intraperitoneal injection with the typhoid bacillus. The injection of 1 to 3000 to 1 to 4000 of the serum by weight into the abdominal cavity will protect against five times the minimum fatal dose, and a dose of 1 to 600 to 1 to 800 of the body weight will protect against seven times the minimum fatal dose of the typhoid bacillus." The writers also state that it has been shown by Ehrlich, Bordel, Wassermann, and others that in artificial immunity the bacteria are destroyed by the combined action of two distinct substances,—namely, the immune body and the complement which is a kind of digestive ferment always present in the blood. The serum with which Stokes and Fulton have experimented is intended to act against the bacilli themselves. Thus far only five cases of typhoid fever have been treated with this serum, and, although the number is too small to deduce any definite conclusions, nevertheless, the effect in three of the cases seemed to be slightly favorable. These investigators have found that it is not difficult to produce a serum of high agglutinative strength and immunizing power by injecting the hog with pure typhoid cultures. Further work will be done on this subject.

DYSENTERY

Shiga, who discovered *Bacillus dysenteriae*, has been doing some interesting work with an antitoxic serum for the treatment of dysentery, and with a prophylactic vaccine. A comparison of the old method of treatment with that of serumtherapy gives the mortality respectively as 35.6 per cent. and 10 per cent. The number of cases treated by the new method, however, is as yet very small in comparison with those treated by the former method. It is to be hoped that valuable results will be obtained in this field, as the disease plays havoc with our army in the Philippines.

YELLOW FEVER

The serum prepared by Sanarelli from *Bacillus icteroides*, as well as the prophylactic fluid, prepared according to Haffkine's method, from *Bacillus icteroides* and *coli* found at autopsies in the liver, heart, and blood of yellow-fever patients, both seem unsatis-

factory. Fitzpatrick, who, with Daly, of New York, has experimented considerably on the subject, summarizes the experience thus far obtained: "The serumtherapy of yellow fever is still in the stage of investigation, and does not appear to warrant any conclusions other than that the blood serum of the *Bacillus icteroides* does not cure nor modify the disease, and that further investigation is necessary."

PLAGUE

Even since the discovery of the plague bacillus great numbers of experiments have been made, especially by Roux and Yersin, to obtain an immunizing and curative serum. Very good results have also been obtained by a number of other investigators, and hopes can be entertained for future success. The reports from the use of Haffkine's serum are very encouraging.

WHOOPING-COUGH

C. Leuriaux (Brussels),² describes an ovoid, aërobic, mobile bacillus which he has isolated from the sputum of patients affected with whooping-cough; it grows rapidly on agar plates, in potato cultures, and in peptonized bouillon. Inoculations of the rabbit, dog, pig, and guinea-pig gave rise, when subcutaneous to violent irritation; when intravenous, to all the symptoms of the disease, and finally to death. Similar phenomena were produced by the toxins secreted by this microbe and obtained by filtration, following the usual procedure of immunizing animals to the poison of diphtheria. Leuriaux succeeded, in the course of from three to four months, in effecting complete immunization of horses to the action of this bacillus and its toxin. As a result of these experiments, he has³ employed with great success the serum obtained in the treatment of whooping-cough, and is able to check the symptoms of the gravest cases in the course of a few days.

It is hoped that these experiments may be verified by other investigators.

Although experimental work is being carried on in the laboratories with the bacteria and sera of scarlet fever and other infectious diseases of childhood, it is still in an experimental stage. Work is also being done on antirabic serum. It is without question of value

¹ *La Semaine Medicale*, July 16, 1902.

² *American Medicine*, August 23, 1902.

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if its use is instituted early in the disease. Many so-called cases of rabies, however, are in reality only cases of pseudorabies.

VENOM AND ANTIVENENE

The conclusions which McFarland gives concerning his investigations with antivenene give much encouragement in the work that has been done and is yet to be done on this subject: "It is not difficult to produce immunity to the nervous poison contained in serpent's venom, as shown by Wolfenden, Phisalix, Bertrand and Calmette. This immunity when carried to a high degree is associated with a marked antitoxic power of the blood. It is very difficult, if not impossible, to produce immunity to the irritative poison of the venom. Antivenene does not protect very powerfully against the irritative poison. It does protect against the nervous poisons of various venoms. Immunity to the unmodified venom is better secured by intravenous than by subcutaneous injection. Calmette's methods of immunization with the modified venom is greatly to be preferred to the method of immunization to the modified venom as tried in these experiments, because of the modicum of danger and suffering to the horses used. It is more useful for the treatment of the bites of cobras and colubrine serpents than for those of vipers, etc. As the antivenene protects against the chief death-dealing elements in the venoms, it is of great use in the treatment of all serious bites, and should be used whenever possible, for the neutralization of the nervous poison of the venom by antivenene will enable the individual to devote all his vitality toward overcoming the local injury done by the irritative globulin in the venom. All individuals—certainly not all horses—are not equal in their resisting power against venom. The antivenene-producing power varies in different horses, while the quantity of antivenene in the blood varies from time to time, according to circumstances." Calmette believes that antivenene serumtherapy presents no very great difficulties. Any one can practise it, and it has become quite common for travellers in the tropics to carry with them the serum and instruments necessary for its use.

Tidswell ⁴ does not believe that any one serum will do for all kinds of snake-bites, as has been claimed by some authors. He has

⁴ Austral. Med. Gaz., Apr. 21, 1902.

taken a number of different serums and treated animals bitten by the tiger snake (the most dangerous of the Australian snakes), and all the animals died. This was also the case in animals bitten by the brown adder, death adder, and black snakes. He then immunized a horse to the bite of the tiger snake and prepared a serum from the blood. This serum would protect animals bitten by the tiger snake, but it would not protect them even when bitten by less poisonous ones, and the result did not seem to bear any relation to the amount of venom or serum administered. The dosage of venom and serum were both carefully studied before the experiments.

A. M. de Moura gives very encouraging reports of the use of rattlesnake poison in leprosy. A steady improvement was noted in all of this writer's cases.

VARIOLA

A specific germ or microörganism of variola or vaccinia has as yet not been discovered. The microörganism of vaccinia exists, however, as is determined by inoculation with the serum or lymph which exudes from the vesicle and its base of the inoculated cow or calf. This organism is also present in the proliferated epithelium. Two substances are used in preparing the vaccine: the pulp, and the lymph or serum. The former consists of the proliferated epithelium along the line of inoculation which has been curreted away from the base, while the lymph or serum is the fluid of the vesicle. In order to obtain these products, calves preferably are inoculated in the abdomen, inner thigh, scrotum, udder or side of the animal with vaccine virus, under strict antiseptic conditions. The vesicle develops in from four to six days, when the animal is secured, the vaccinated surface thoroughly cleansed with sterile water, the scab or crust removed, the elevated ridges curetted, the scrapings or pulp thoroughly ground and mixed with glycerin, usually 60 per cent., in the proportion of one part of pulp to three or five parts of glycerin. The mixture is stored for a month before it is used. One part pulp to ten or even twenty parts of the diluted glycerin is said to be quite efficient.

The fluid lymph is allowed to dry on ivory or bone points, which are dipped in the serum as it oozes from the vesicle.

The vaccine used to inoculate the animals is that descended from spontaneous cowpox through an indefinite series of animals, and this is the true animal vaccine. Or it may be obtained from animals

which have been inoculated with lymph from human vaccine pustules, directly or indirectly through a number of animals. This is designated retrovaccine. Again it may be obtained through the passing of smallpox virus through the cow or calf, and this is known as variola vaccine.

Both of these preparations are successful in conferring immunity to smallpox in the human subject. The vaccine derived from the pulp, however, is considered richer in the specific virus than is that of the lymph, and with longer action, but does not retain its activity for as long a period as the lymph vaccine. The period of activity for the points is dependent upon the amount of heat and moisture to which they are subjected.

The technic for the use of vaccine includes the proper selection of the lymph, the condition and age of the patient, the insertion of the virus, and the care of the wound. Vaccine made under State control should, if properly safeguarded, be as near ideal as it is possible for a preparation of this kind to be. If control tests are undertaken by killing the animal after the virus has been secured and carefully examining the carcass for disease, if the virus obtained from the animals showing the least evidence of disease is rejected, and if great care is used in preparing the lymph, the percentage of unpleasant complications or failures should be practically nil.

If the State enacts laws compelling vaccination and insists upon it without regard to personal prejudice, it should furnish the vaccine and guarantee its purity and efficiency, or else be held responsible for any disaster. Liability of the State is insisted upon in many ways when negligence is in evidence. When this is so in a commercial or material way, and is so held by the courts of justice, is it not monstrous to have a court declare a municipality irresponsible morally or legally when a product manufactured by their own servants is destructive of numbers of children through gross and inexcusable negligence of these officers employed to guard against such accidents?

Children under 3 months of age should not be vaccinated unless in the midst of an epidemic, nor while undergoing the process of teething. It is also unwise to subject to vaccination a child suffering from some constitutional disease or inflammatory skin trouble, such as eczema, erysipelas, etc.; or if it recently has been exposed to

infectious disease, such as scarlet fever, measles, mumps, or whooping-cough. Revaccination should occur when the child has reached 12 years. Vaccination should be practised only under the strictest surgical asepsis. The skin on the arm or leg of the patient should be washed thoroughly with soap and water, dried and afterward rubbed with alcohol or ether. Scarify the skin with an ordinary needle previously sterilized by heating in the flame of an alcohol lamp or Bunsen burner, apply the lymph and prick it with the needle into the scarified places. If several insertions are made, they should be an inch apart, to avoid the coalescence of the vesicles. The lymph should now be allowed to dry before the spot is covered with the clothing. No protection is needed, but if used should consist *only* of a bandage of sterilized gauze. There is no necessity for the operator's fingers coming in contact with the skin of the patient at any stage of the process of vaccination.

The care of the wound should not entail annoyance if the operation has been properly done and the vaccine used was of the proper quality and free from bacteria. Should the vesicles break down and suppurate, they must be cleansed daily with sterile water, covered with a mild antiseptic, and kept protected with sterilized gauze. The patient should be warned not to interfere with the vesicle through picking at it or scratching it, nor should any oily or greasy substance be applied.

The complications most apt to occur in vaccination are erysipelas, urticaria, impetigo contagiosa, enlargement of lymph glands, tetanus, and cellulitis. These when they occur are the result of a faulty technic—lack of perfect antiseptic precautions—or to some disturbing element in the virus. Bacteria, such as staphylococci, streptococci, etc., together with various fungi and yeasts, have been repeatedly demonstrated in both forms of vaccine. Of 41 points examined by Rosenau, an average of 4807 bacteria were found on each point, and of 51 tubes of the glycerinated virus an average of 2865 bacteria per tube were found. How to avoid these bacteria, some of them pathogenic, is a problem for State bacteriologists to determine. That this should be and can be accomplished is reasonably certain.

Immunity.—It would seem superfluous at this day, and with a century's experience behind us, to dilate upon the immunity to smallpox conferred by inoculation of vaccine virus. That the dread-

ful ravages of this disease have been placed under control must be admitted by any one who is at all acquainted with history. As to the transmission of other diseases through the virus, we are not prepared to state conclusively that such transmission does or does not occur. Whether the increase of tuberculosis and cancer is in any degree dependent upon the prevalence of vaccination must be left to statisticians and investigators to come. Granting, however, that such diseases can be transmitted to man, we must accept the fact that smallpox is no longer the terrible scourge it was before vaccination was practised, and that many lives have thus been saved. The rule, therefore, in this must apply, that whatever is best for the greatest number must be accepted as good. If tuberculosis and cancer are in any way due to vaccine, the percentage must be immeasurably small, in fact, of little consequence, when compared to the blotting out of the smallpox scourge.

Medicine

MUCOUS COLIC, OR MEMBRANOUS COLITIS

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CASES of mucous colic vary very much in the severity of their symptoms. Milder ones are not very uncommon, but the severe are only infrequently met with. The essential symptom is the occurrence of mucus in the stools, usually with pain, which is often severe. The mucus may be soft and grayish, or condensed into white, dense flakes, shreds, or long bands, and occasionally into well-formed casts of the bowel. All these variations in the evacuations may occur in the same case. In most cases the attacks are periodical, often with complete absence of either mucus or colic in the intervals, as illustrated by the following case:

Mrs. W., aged 44 years, was a rather stout, pale, yet fairly vigorous looking woman. Her last labor occurred 14 years ago; it was difficult, and followed by pelvic abscesses. Since then she has been subject every four to six weeks to severe attacks of colic, with copious evacuations of shreds and bands of dense, white mucus, but no gelatinous material. In each attack there has been marked pain of a colicky nature lasting throughout it. After a few days the attack abated, and there was comparative comfort during the interval. The bowels were constipated and quite difficult to move, the stools being hard and often showed adherent mucus. In the attacks the stools were partly liquid and partly scybalous. Small streaks of blood were present frequently, and on the last occasion the bleeding was fairly free.

She was a woman of nervous temperament, easily disturbed by even slight ailments. Her digestion was fair, although the food remained somewhat too long in the stomach, which was thus shown to be atonic. It was prolapsed, so that its greater curvature was

below the umbilicus. She suffered much from neuralgia of various parts, chiefly the head, where it often began as hemicrania. There was much backache, and on pelvic examination the uterus was found displaced backward, and markedly tender on each side. Menstruation was regular and not very painful. The urine was usually scanty before the attacks, but copious and pallid during and after them.

There was not an opportunity of examining the mucous discharges, but, in the absence of any other evidences of inflammation of the bowels, there is little doubt that they showed no signs of being due to inflammatory process. The blood probably came from some of the small hemorrhoids, of which there were several in the rectum.

In some cases, instead of periodical attacks, the trouble is persistent but variable, as illustrated by the following case:

Mrs. T., aged 55 years, of good personal and family history. She had two children, both dying in childhood. Menses had ceased at the age of 51 years. The urine was normal, but the bladder had been irritable for over a year. All her organs were healthy. She was rather fat (weighing 158 pounds), nervous, easily fatigued, and much concerned about her ill-health. Her pulse was easily excited, and she was much constipated, the bowels being difficult to move, and mucus, usually in long bands and shreds, was present in the stools, which always contained large, scybalous masses. Frequently, before and during the movement of the bowels, the pain was severe. It usually began in the left side and radiated over the whole abdomen. The more copious the evacuation the greater the relief that resulted. She had been suffering for three years without any intervals of complete relief. She complained much also of constant rectal fulness and tenesmus.

The abdomen was full and held rather rigidly. It was tender in the region of the descending colon chiefly; in a less degree and less constantly in various other parts also. The abdominal wall was too thick and rigid to permit of the colon being palpated. Her appetite was good enough, but digestion was defective, although not attended by material discomfort, except much flatus. Three hours after a breakfast of one egg, toast, and coffee there were several ounces of food still in the stomach, and free hydrochloric acid was present in excessive quantity. There was some prolapse of the stomach, and

probably of the other abdominal organs, but such could not be demonstrated.

The shreds and bands were found to consist of condensed mucus, with no inflammatory products, and but little foreign substances from the cellulose or other constituents of the food.

These two cases serve as types of this peculiar disease. Both patients were quite neurotic and subject to various nervous affections, but otherwise they were in fair general condition. In both there was constipation, as is almost uniformly true of these cases. In one the mucous discharge was variable, but persistent; in the other it was periodic. In both, digestion had long been defective, there being atony of the stomach and marked increase in hydrochloric acid secretion. In the second case only was there an opportunity of examining the discharges, and they were found to consist of condensed mucus without any signs of inflammatory exudate.

In most, and probably all, cases, as in these two, the condition is due to a neurosis, which causes an excessive secretion of mucus, and to spasmodic contraction of sections of the colon. Above the seat of spasm the mucus is retained and may be condensed into shreds and bands, or even into casts. In many cases, however, the mucus, as secreted, is in membranous form, intimately adherent to the wall of the bowel and difficult to separate. In such cases the formation of membrane is not due to retention, but to alteration of the character of the secretion, and doubtless may be found without the occurrence of spasm. The bowel above the seat of spasm is atonic and may become dilated by the retained feces. Sacculi of the bowel may form, in which scybalous masses may lodge indefinitely. The atony, sacculi, and spasm of the bowel afford ample explanation of the constipation, the scybala, and the difficulty in securing free evacuations.

By many a separate class is made of the cases in which there are evidences of inflammatory or other lesions of the colon, and they attribute the mucous formations partly to nervous and partly to anatomic causes. Few hold with Boas that organic disease alone is sufficient, while few doubt that many cases are due to nervous causes alone. Cases are reported in which at autopsy membrane has been found intimately adherent to the mucous membrane of the bowel, which, on removal of this adherent membrane, showed no

trace of disease. It seems then not unreasonable that even in the presence of organic disease the mucous formations are still due to nervous influence. In the case of a neurotic young girl with abdominal disease, probably tuberculous, at present under observation, two attacks of mucous colic have occurred while at home. While suffering from the first she was removed to a hospital, and the mucous discharge ceased at once. After her return home some months later a second attack occurred. In both attacks the neurotic disturbance was very marked, and cessation of the mucous discharges was coincident with improvement in the mental condition, although there was then no improvement in the symptoms of the organic disease. It is evident that these mucous formations do not occur apart from the neurotic state, and, as in the majority of cases there is no organic disease to cause them, there seems no doubt that they result from a secretory neurosis.

In the *treatment* of mucous colic the neurotic state should be kept in mind as well as the bowel affection. In many cases a cure will follow an improvement in the mental state resulting from a change of scene, removal from depressing surroundings or the overzealous attention of friends. Probably not a few of the milder cases recover under reverses by which they are compelled to assume responsibilities, even to the overtaking of their energies. In well-marked cases the Weir Mitchell "rest cure," modified to suit the individual patient, especially with reference to the neurasthenic symptoms, gives the best results. If the neurasthenia is only slight, complete rest in bed for a week or two may suffice, after which moderate exercise may be advisable, according to the progress.

In the treatment of the bowel symptoms the object is to stay the attack as soon as possible and prevent its recurrence. To do this rest in bed is of the first importance. To allay the pain hot applications should be made to the abdomen, either moist or dry, as most convenient, heat being the important agency in relieving the sectional spasm of the colon, to which the pain is due. This is usually insufficient, and an anodyne is required to relax the spasm and relieve the pain. A hypodermic injection of morphin is, of course, the most rapid and effective, and should be given in at least all severe cases. By relaxing the spasm it permits the bowel to move and may be thus the best purgative, as without relaxation of the spasm no purgatives can act efficiently. At the same time a copious enema

may be given to sweep out as much as possible of the mucus and fecal contents. The more thoroughly the morphin relaxes the spasm the more thoroughly can the enema empty the bowel. If the spasm is not relaxed the enema can only affect the bowel below its seat, and it may aggravate the spasm and increase the pain. Even in the most favorable cases all the mucus cannot be got rid of by one treatment, especially if it is in the form of adherent membranous deposit.

The second case above detailed illustrates the efficacy of this plan of treatment. She was put to bed with heat to the abdomen. One-sixth grain of morphin (0.01 gram) was subcutaneously injected and a high enema given. Much fecal matter, including scybala and mucus, gelatinous and membranous, was passed. At bedtime another hypodermic injection of morphin was given to insure complete relaxation of spasm and a good night's rest. A pint of warm olive oil was injected as high as possible into the colon and allowed to remain over night, in order to separate the adherent mucus. She rested well until early morning, when the bowels moved, a copious, simple enema being given as soon as symptoms of movement began. The evacuation was large, and contained much mucus in shreds and gelatinous masses, and many scybala.

Following von Noorden's advice, a coarse, vegetable diet was given, with much butter and fat bacon, to furnish the intestine a large quantity of coarse material to stimulate peristalsis. The fermentation of the cellulose of the fruit and vegetables tends to prevent the fecal material being condensed into scybalous masses, as do also the fats. Sulphur at night and Homburg salts in the morning were also given to aid in keeping the feces soft and securing free evacuation.

The abdomen was thoroughly massaged daily to stimulate peristalsis, and also to displace fecal and mucous collections that might be lodged in dilatations of the colon above the seat of spasm. After three days of such treatment, during which the bowels were moving two or three times daily, large scybala, which could not have been formed during this time, were passed. They must have been lodged in dilatations above the seat of spasm. After the first day suppositories of opium and belladonna were used to allay the pain. By the end of a week pain ceased and mucus disappeared from the evacuations. The treatment was continued, except that opiates were withdrawn; she was allowed to sit up, and in a

day or two to go out driving, and later walking. She returned home at the end of a month quite relieved. The quantity of coarse vegetable food was to be gradually reduced and ordinary food substituted. As a substitute for massage she was advised to exercise the abdominal muscles systematically morning and night in order to improve the tone of the abdominal wall and thus afford better support to the contents of the abdomen. For this there was much need, as there was considerable prolapse of the stomach and other organs; the abdominal veins would also be benefited by firmer and more active abdominal support.

She has since remained in good health, but, of course, if she yields to depressing conditions and neglects the means of preserving a good physical condition, there may very probably be a recurrence of the bowel trouble.

INJURIES AND LESIONS FOLLOWING THE TOXIC USE OF ALCOHOL

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EVERY year the clinicians are able to trace mental and nervous diseases more clearly to distinct causes, such as injuries, concussions, brain-shocks, heat-strokes, and sun-strokes, alcohol, syphilitic and other infections. Sometimes the connection between these causes and the diseases which follow are very clear, and can be traced in a continuous line of symptoms. In other cases the connection is obscure, there are breaks in the history, and yet the inference that these causes are the starting points of disease is beyond question or doubt. Syphilis and alcohol are now recognized as among the most prominent, active, and predisposing causes of nervous diseases. When they can be eliminated in the study, both the diagnosis and the prognosis are much more favorable. As a rule, alcohol is used either to intoxication at intervals or in moderation daily.

Familiarity with states of intoxication and the delusive theories of moral causation have not only repelled, but obscured, the study of the pathology and psychology of this form of poisoning. Delirium tremens and delusional alcoholics seen on the street and in the police station-houses are literally more obscure and less known in their etiology and pathology than yellow fever or the plague.

I shall divide the present study into two parts: (1) A consideration of the injuries and lesions which occur in persons who use alcohol to intoxication, that is, who become visibly poisoned by spirits, and manifest this in extraordinary conduct, delirious talk, and states of palsy, which pass off after a time; and (2) a consideration of persons who use alcohol moderately, by which I mean those who use spirits in small quantities at meals or at other times, seldom exceeding a given amount.

In the first class, I shall note special forms of injuries which follow from the toxic use of spirits; in the second, diseases and injuries which have come on gradually and are due evidently to the

toxic action of spirits. As an example of the first kind, a physician, after a banquet, during which he drank several kinds of wine, was conducted home in a state of stupor. Later he developed convulsions, followed by profound collapse. He had been a total abstainer, had lived a regular life, and this was the first intoxication, and practically the first use of spirits. He recovered in a few days, and later developed insomnia and acute nervous dyspepsia. A year afterward his mind and body became very feeble. Neurasthenia and paranoiac delusions were diagnosed. Later angina pectoris developed. After three years of profound invalidism and psychic disturbance, he died from acute pneumonia. There was every reason for believing that the toxic action of alcohol was the exciting cause of the disorders and diseases which followed.

A second example was that of a business man who had always refrained from the use of spirits and tobacco. He passed a rigid examination for an insurance policy, and a week later, while crossing a river in a boat, he fell overboard, and remained in the water a long time, and was thoroughly chilled before being rescued. He was given large quantities of hot spirits, and in a short time became intoxicated and delirious. Opium was given to quiet the delirium, and then more spirits to overcome the weakened heart's action. A severe illness with mental disturbance followed and lasted six weeks. Finally he recovered and went abroad for a rest. He used wine at meals during his foreign travel, and he came back without any improvement. Later acute dyspepsia, palsy of the lower extremities, insomnia, tachycardia, and cirrhosis of the liver appeared. He was treated continuously for the next five years by different physicians, who were unable to make a positive diagnosis, and finally he died from some unknown disease. No one suspected that the toxic action of the spirits after the sudden chill had anything to do with the subsequent degeneration and disease.

A third example was that of a clergyman, 30 years of age, who was a strong athletic man, with no history of disease. While traveling in the country he was bitten by a snake and was treated with large quantities of cider brandy until he became profoundly intoxicated. He remained in bed for a week, during which time brandy was given freely. Then he recovered. Six months later he was treated for rheumatism, nervous exhaustion, brain fatigue, and profound dyspepsia. A number of physicians examined him, but

no definite diagnosis was made. A year or more afterward nephritis with persistent anemia and insomnia was diagnosed. After a varied treatment extending over two years, he died from cerebral hemorrhage. It was ascertained that the snake bite was from a harmless species, and the subsequent disease seemed due to the action of spirits, which began at the time of the snake bite.

Examples might be multiplied almost indefinitely in which it is apparent that profound poisoning from spirits injures the neurotic and nutrient centers and is an exciting cause of the diseases which follow. Fortunately, alcohol is not used as heroically for medicinal effects as in former days, otherwise such examples would be common. Cases of so-called rheumatism, which are often practically neuritis, are traceable to the excessive use of spirits frequently taken for some medicinal purpose. The palsy and mental disturbance which follow are ascribed to causes other than the real one. In some instances persons who are depressed or shocked from fear or sudden mental perturbation are given large quantities of spirits and become intoxicated. The alcoholic poisoning at this time seems far more severe and protracted than when taken under other conditions. Many chronic inebriates give a history of having first used spirits after some shock, extreme excitement, depression, or condition following heat- or sun-stroke. The toxic states which followed created a desire for spirits so pronounced and impulsive that it could not be given up. Here it was evident that the use of alcohol was both an exciting cause and symptom of some change dating from the time of the injury and the first use of spirits.

There are clearly many states of the body in which the toxic action of spirits is notably degenerative in its effects from the beginning. I have made some studies of dipsomaniacs and periodical inebriates who have taken large quantities in the invalid stage following typhoid fever, pneumonia, and influenza, and it was evident that alcohol used at this time for its supposed tonic and stimulant action was in reality an active cause of mental and physical diseases.

Obstinent dyspepsias and nutrient disturbances are traceable to profound intoxication or to periods of severe drinking under special circumstances. Thus, after a period of gormandizing, the person suffers distress and uses spirits for relief. He has acute indigestion and severe prostration, after which follows a train of symptoms

showing central brain disturbances which demand the continuous use of spirits.

A second division of the first class are persons in whom spirits are used to intoxication, followed by distinct free intervals for some length of time. Many marked neuro-psychoses and psychopathies are traceable to toxic states due to spirits. In some there is at first a marked aversion to the taste and effects of spirits, but after a time this is overcome; then acute symptoms follow, and are often more serious than in other cases. Very early sclerosis of the liver and kidneys appear, with a marked disturbance of the heart action; then later marked neuroses and local palsies come on and are ascribed to causes other than the spirits. If malaria or syphilis has existed in the past, they are supposed to be prominent as active causes.

Many of these persons suddenly develop very unusual symptoms, which are variously diagnosed and treated for a period of time without results. The following is an example:

A young man of good health and no neurotic heredity became profoundly intoxicated on the day of his graduation. He was delirious, maniacal, and stupid for two days, and then recovered. For the next ten years he was a hard-working, temperate man; but he suddenly became prostrated, both in mind and body, gave up all business, and remained in bed for days at a time.

The physician regarded this as hysteria, and later considered it congestion of the brain. After three months he recovered. The next year a similar attack of obscure mental debility followed. For some unknown reason he drank to intoxication, and all symptoms of debility passed away, and he resumed his accustomed work. For five years following he drank steadily, and then died from acute pneumonia. There seemed to be a very close connection between the shock and the injury from the first intoxication and the later neurotic exhaustions and final development of inebriety, although not recognized by the medical attendants. Many persons who, after a period of invalidism and apparent exhaustion, become moderate or excessive drinkers, or take drugs, are often found to have an early history of some profound intoxication. The connection between these first toxic states and the later conditions, although obscure, is often traceable.

We are all familiar with a class of nervous patients whose ail-

ments are obscure and who visit various doctors and institutions, receiving little or no benefit, and finally die of some acute disease or supposed heart-failure. Many terms have been used to designate these cases, prominent of which are brain fatigue, nerve exhaustion, and certain germ diseases, but there is always an obscurity and complexity of symptoms which cannot be understood. Many of these persons will be found to have had at some previous time severe toxic alcoholic poisoning, and from this there was an apparent injury, manifest at first by increasing nervousness, loss of concentration, morbid fears and disinclinations, and other symptoms of weakened brain and nerve power. These obscure neuro-psychopaths, after periods of alcoholic excesses, have seemed to recover, and later disturbances were ascribed to recent causes and not to early poisonings. Many persons who drink to intoxication at long irregular intervals and then recover, and who are classed as temperate men, complain of rheumatism, heart failure, and other vague and uncertain disorders. Probably the first is neuritis, which after a short period subsides, leaving chronic conditions of pain and stiffness of the joints. A physician who had drunk at intervals strong spirits for several weeks, then abstained, was finally taken with what he called acute articular rheumatism, and, after suffering many months with severe pains in the legs, associated with heart depressions, died. There was no recognition that his death was due to alcoholic drinking, yet the post-mortem revealed a multiple neuritis in the nerves of both hands and feet.

Every toxic poisoning from alcohol is both a physical and psychical concussion to the brain-centers, and is the beginning of both organic and functional changes which may go on rapidly or slowly to serious degenerations and diseases. Frequent intoxications so depress the brain-centers that a condition called dementia is encouraged and may begin, although concealed for a long time. A careful study of persons who use spirits continuously or to excess at intervals show prominent organic changes, with feeble resisting power and increasing susceptibility to the toxic effects.

As remarked before, each toxic action is practically a concussion which culminates in and finally becomes well-marked organic degeneration. While the phenomenon of intoxication is more or less familiar, its physiologic and pathologic significance is largely unknown. An enumeration of the common symptoms following the

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use of alcohol will give some indications of the profound changes of which these are only hints and signal-flags.

The first effects of spirits are flushing or blanching of the face, due to disturbances of the vasomotor control. A little later, after the period of agitation is passed, the facial muscles become fixed and have a stolid, palsied appearance. The first emotional play and the red flush passes away, settling into a stolid, fixed state, the face becomes pale, the lips more firmly compressed and when used have a spasmodic, jerky movement. The eyes at first appear bright and glittering, then become suffused with tears, and roll about in an unusual way, or settle into a fixed palsied look. The voice is altered, articulation is rapid at first, then slowed down. The words run into each other and are uttered with more or less effort. Respiration is quickened, and a sense of shivering and agitation pervades the body. The brain activity is suddenly increased, then gradually becomes less, and finally merges into confusional states, with difficulty of utterance, during which all the former symptoms disappear and the brain seems to be struggling to express itself. The first effect of spirits is like a shock and a sudden interruption of the normal, rhythmical flow of nerve energy and thought; then comes a delusional, jerking, erratic period. With this there is profound alteration of the direction and movement of the functional activities of the brain. Later the special senses are impaired, sight is diminished, the hearing is dulled, touch, taste, and smell are all lowered. There is a fall in the temperature. The muscular power is enfeebled and memory is weakened. Rapidity of thought and power of concentration, with conception and perception, all seem more or less paralyzed.

There is a period of emotional exaltation and delusional confidence to think and act more wisely and clearly. This is followed by an anesthetic period in which depression and feebleness of the sense centers appear. These finally develop into stupor, palsy, and unconsciousness. The so-called stimulating period is irritation, and really the first stages of paralysis. Psychologic measurements of the brain and sense functions, as well as the organic activity, show palsy and lowering of acuteness, and yet the theory of stimulation and increased vigor has been accepted and used as if it were a certain fact.

Professor Wood calls the toxic poisoning from alcohol a paraly-

sis of the nerve and brain functions. The feeling of comfort and exaltation are found to be literally delusions. Associated with this feeling are always degrees of palsy of the senses, reason, and judgment. Later, when the effects are worn off, headache, general debility, with irritation of the stomach, are significant signs of injury. These and other symptoms seem to call for more spirits to cover up the pain impressions. The craving for spirits, following the toxic stupor and anesthesia, is a symptom of the damage done; the apparent result following has been simply covering up and increasing the degeneration.

A very interesting study was made by the late Dr. Kerr of ten average business men who used beer and spirits continuously for periods of twenty or more years. There was no reason to believe that any one of this number had been intoxicated during this time or had suffered from the extreme toxic action of alcohol. All claimed to be moderate drinkers and never to take over a certain minimum amount. Four of the ten died from pneumonia suddenly. Two had hemiplegia two years before death, and one died of apoplexy coming on suddenly. The other three had a period of invalidism following nephritis and gastritis, and one died of dropsy. In the judgment of the friends and relatives, six of these persons were invalids, and debilitated for the last four years of their life, being under the doctor's care very often. Two of them complained of malaria, and attributed many symptoms to this cause. Six of them suffered apparently from rheumatism, the symptoms of which were pain in the legs and feet, with stiffness and swelling. His final conclusion was that each one of these persons suffered for years from toxemias, paralysis, and defective nutrition, due directly to alcohol. They were all active business men, and so far as known lived quiet, regular lives. An example of this class came under my care for advice. He suffered from paroxysmal attacks of indigestion, insomnia, and general prostration. His memory was weak, and for years he had been gradually losing flesh. The kidneys at times seemed to be disordered, and both sugar and albumin were found. Nervousness and heart weakness were prominent. He had tried various methods of nerve-rest, water-cures, sanitarium treatment, and journeys abroad, and consulted with different physicians without relief. He was accustomed to using wine at the table three times a day, and small quantities of spirits nights and mornings. At no time, from

his own statement, was he aware of any toxic action due to these drugs. Absence from all spirits and an active course of hydropathic measures resulted in complete restoration, and now, after a period of five years, he is practically well and able to carry on a large business. This case is a common example of those of which the real cause is spirits unrecognized. Surgeons and clinicians have for a long time recognized practically the low vitality and deficient recuperative powers of alcoholic persons, particularly those suffering from traumatism or acute fevers.

The prognosis in such cases is always graver and the complications more pronounced. Marked examples of this have been repeatedly noted in the hospitals in Liverpool and London and other cities of Europe, particularly among persons of the working-classes who have used large quantities of beer and who are admitted for injuries or fevers. The mortality from injuries and fevers is double that of persons who are abstinent, and yet many of these persons are not of the drunkard or inebriate class. They are simply moderate beer- and spirit-drinkers who continue their work daily, drinking regularly and living otherwise temperately. In such cases traumatisms frequently develop gangrene, and the shock of operation has a particularly depressing influence on the vitality, lowering it beyond the power of restoration. It has often been noted that when spirits were given as a stimulant the inflammatory processes were increased and the heart's action diminished. In fevers the temperature is made higher by the action of spirits and the heart's action more unsteady. This experience is confirmed in the hospital practice of all large cities, and, while spirits are still given for stimulant effect, surgeons and clinicians are substituting strychnin and other drugs as being more certain and less injurious.

Some very interesting studies have been carried on by the American Association for the Study of Inebriety and of the work done in fields of science and literature by persons who use spirits in moderation or to excess. A large amount of data has been already accumulated, but the conclusions are not yet published.

Among the facts which seem to be established is, that alcohol used regularly in any form or degree of moderation is depressing to the brain and nervous system and lowers the power of original investigation and logical research, and, at the same time, obscures the judgment and deceives the investigator so that he is unable to

judge of the value of his own work. One of the very striking examples confirming this was that of a noted astronomer who, from the advice of his physician, began to use wine at meals. He was exhausted, could not sleep, and suffered from obscure symptoms which were called nerve fatigues. He continued his work for several months, using spirits daily, and feeling very much better. Then he was sent away on a commission, and the work of the past three months came under review by another astronomer, who found it very faulty. On his return he was asked to review his work, which was largely mathematical. He found it practically worthless, not only in errors of observation and conclusion, but in the deductions from the facts which he could not discover at the time.

Experience in business and professional circles requiring exact and accurate work confirms this conclusion, in showing the failure of persons who use spirits to do the best work mentally and physically that they are capable of. There is no theory or sentiment in this other than the conclusions and teachings which are founded on hard and inexorable facts.

There are some conclusions which may be stated with great confidence as sustained by clinical experience and study, as follows: Intoxication from the use of alcohol (meaning states of stupor and delirium directly due to this cause) is far more injurious to the brain and nervous system than modern teachings and text-books would indicate. This is not seen in individual cases, but in the aggregate, and in the after history of a large number of persons who have been intoxicated repeatedly from alcohol. There are lesions, injuries, and defects of both the brain and nervous system that are clearly due to this particular cause. The fact is well attested that profound intoxication at or about the period of puberty is the starting-point of disease and degeneration appearing in after life.

Intoxication for the first time in middle or later life is often followed by most serious entailments which are seldom attributed to this source. Many observations have shown that toxic states of alcohol following diseases, injuries, and great mental strains seem pronounced causes for the intensification and localization of psychoneurosis of great variety and form.

When the use of spirits has reached the spasmodic or the epileptoid stage described by the term periodic, which means a maniacal

impulse, and the subject uses spirits for its narcotic action for a certain distinct period, which is followed by revulsion and a period of total abstinence, central organic stages are present. This condition is a very serious one, and it must be recognized in the study and treatment of disease. Its significance is even more prominent than that of syphilitic infection. The use of alcohol continuously in moderation for long periods has a cumulative action that is practically unknown, and only recognized by the clinician from accurate studies of the causes of diseases. Undoubtedly a certain proportion of the active brain-workers and so-called healthy men in middle life use spirits in some form either continuously or at intervals.

The question how far this use favors degeneration, encourages disease, lowers vitality, increases mortality, and otherwise produces most injurious effects, is open for study and examination. That its influence and effects in certain cases are very pronounced is established beyond doubt. The cumulative depressing action of alcohol, calling for its renewed use on and on until death follows, is observed in every community. Like opium, the anesthesia and narcosis from its use imperatively demands more and more. Hence its cumulative action, whether recognized or not, is present, and it is exceedingly doubtful if there is any point in its use where its beneficial and injurious effects join. It can be stated with great positiveness that very serious neuroses and organic changes follow from the action of alcohol on the brain and nervous system; also that a large part of the neuro-psychopathies and complex disorders are traceable to this cause, not always primary or specific, but as exciting and predisposing. Lastly, the poisoning from alcohol is far more serious in its effects than is at present recognized, and the field for study in this direction promises a great revolution in the etiology and diagnosis of disease.

ULCER OF THE STOMACH, WITH CONTRACTIONS, IN A BOY AGED FOURTEEN YEARS; CEREBRAL HEMORRHAGE AND LUMBAR PUNCTURE; CURA- BLE ALBUMINURIA ¹

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ULCER OF THE STOMACH

CASE I.—The first case to which I ask your attention, a case of ulcer of the stomach in a boy, aged 14 years, belongs to the class called rare. In fact, some authors claim they never occur; but we have indisputable evidence that they do. And in detailing this case I must differ with my friend, Dr. Hugh T. Patrick, who is quoted as saying, "If we would put more time on cases of which we see one in a lifetime, it would be of great benefit to ourselves and to our patients." While this dictum is in the main true, it is the study of the rare cases which broadens the field of diagnosis. For instance, in 1875 Sir William Gull read a paper on "Cretinoid State Supervening in Adult Life in Women," and in 1878 Dr. Ord discussed the pathology of the disease and gave the name myxedema to this cretinoid state. In passing, I will say that in 1881 I reported the first case of myxedema, so far as I know, that has been reported in the West. And since that time the theoretical views of Ord as to the pathology of myxedema and other cretinoid states have not only been confirmed, but the real pathology of the disease has been established; and the thyroid therapy has been of vast benefit to thousands of patients who would otherwise have been doomed to idiocy or imbecility. How many cases of starvation from unexplainable causes have been observed among infants and children in the past? The researches of the past few years have established the fact that stricture of the pylorus is not an uncommon and irremediable condition. In 262 cases found in the Berlin Pathologic Institute, no cases

¹ Read before the Scott County Medical Society, Davenport, Iowa, April 25, 1905.

of ulcer of the stomach in patients under 10 years of age were found. Nothnagel in his series of 260 cases does not state the youngest age at which he has found the disease, but states that he found 43 cases in patients under 20 years of age. Kundrat states that it is not uncommon to find ulcers as small as a millet-seed in children and infants; he assumes that these ulcers are the result of hemorrhages, but he admits that he has never known them to develop into chronic ulcers under 10 years of age. Widerhofer states that gastric ulcer never occurs in childhood; but, according to Henoeh, ulceration of the gastric mucosa is often found in the new-born. Ertheimer reports a case in a child of 10 years, and Eross one in a girl of 12 years. The literature, therefore, is free from frequent reports of cases, but it is my opinion that more careful study of these cases in the future will enrich our literature with many more cases.

I am indebted to Dr. George W. Newton, of Chicago, for this patient, whom he referred to me at the Presbyterian Hospital, he having made a diagnosis of ulcer of the stomach, and suggested removal to the hospital in order that the dietetic and hygienic management might be more thoroughly carried out than was possible at the patient's home. Dr. Newton stated that the boy had been ailing for about one year, the first symptoms being pain after eating, a sense of fulness of the stomach, followed later by vomiting of mucus and blood, the vomiting becoming more frequent, and the patient quite rapidly emaciating and becoming anemic. In January, 1904, he weighed 96 pounds. At that time the discomfort came on about three hours after eating. But as the disease progressed the pains, vomiting, and nausea came on soon after eating. A point of tenderness under the ensiform cartilage was found, and the patient was placed on rectal feeding, complete rest in bed, and nitrate of silver internally. For some months he improved. Toward the end of November, 1904, contrary to orders, he was allowed to partake freely of solid food, and, soon after the Thanksgiving Day dinner, he vomited about one-half cupful of bright red blood. From this time the patient progressively failed, and was finally sent to the Presbyterian Hospital, weighing 37 pounds, and having the emaciated appearance as shown in Fig. 1.

On admission the physical examination was negative, so far as the circulatory and respiratory organs were concerned. There were glandular enlargements. The liver was not enlarged; the spleen was

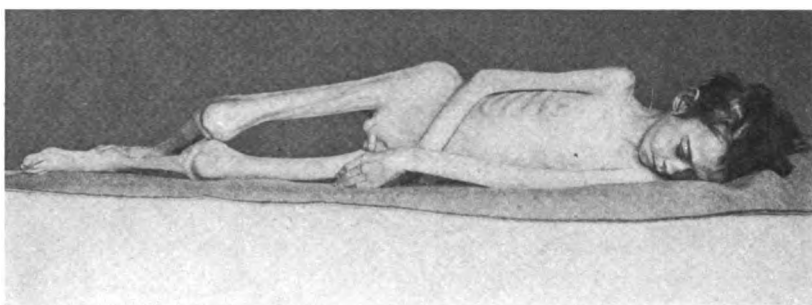


FIG. 1.—Showing extreme emaciation in a boy, aged 14 years, the subject of ulcer of the stomach.

not palpable. The boy could swallow liquids if the liquid was taken slowly, but only in small quantities. If an attempt was made to swallow solid food it would be immediately regurgitated, the food coming up without any apparent effort. The food when regurgitated was enveloped in large quantities of mucus, and occasionally streaked with blood. Every endeavor to pass an esophageal sound was a failure, the bougie stopping apparently about an inch from the cardiac extremity of the stomach. Catheters of the smallest caliber would not pass. The patient weighed 37 pounds the day before his death, not having gained an ounce during his two months' treatment in the hospital, notwithstanding he had apparently ingested large quantities of nourishment and had been fed per rectum.

At the autopsy the body measured 149 centimeters in length. The abdominal and pleural cavities were empty and free from adhesions. There were a few delicate, easily torn adhesions in the lower peritoneal cavity. The foramen of Winslow was patent. The stomach was vertical and much contracted, measuring 5 centimeters from cardia to pylorus, and 2.5 centimeters transversely. The first part of the duodenum was somewhat dilated. The bile duct was patent and emptied 10 centimeters below the pylorus. The omentum was normal in its relations to the stomach. The cardiac orifice of the esophagus was narrowed, and its internal circumference was 4 millimeters. There was a subdiaphragmatic esophageal diverticulum 3 centimeters below the constricted point, and 1.5 centimeters below the opening into the stomach. The opening into the stomach measured 1 centimeter in circumference. The lining of the stomach was fibrous tissue. There was an ulcer at the pylorus extending nearly around the pylorus and 1 centimeter broad. The wall of the stomach measured 4 to 8 millimeters in thickness. The mucosa of the duodenum and intestines showed no change. There was general lymphadenitis. The lower lobes of both lungs were edematous and congested. The liver and kidneys showed cloudy swelling. The other organs showed no changes, either gross or microscopic. The sections of the walls of the stomach showed scar tissue, replacing the mucosa and submucosa, especially in the region of the cardia. Sections of the ulcer show a dense infiltration of the mucosa and submucosa. Culture-tubes inoculated from the bile remained sterile.

Before the esophagus was opened it was impossible to get a

bougie, water, or air through it, showing a dense, fibrous constriction existing in the lower end. On section two strictures were found, one about 2 millimeters, and one about 6 millimeters, from the cardiac end of the stomach. The stomach was contracted, the pyloric extremity had a great deal of dense fibrous tissue, and the pyloric end was constricted. The pathologic findings demonstrate perfectly the cause of the food regurgitation and the failure to nourish the patient.

That this was not a case of congenital disease of the stomach is proved by the fact that the patient was apparently well until about one year ago, when the first evidence of disease appeared, and the case then had the usual clinical history of an ulcer of the stomach.

The question which naturally arises is, Suppose the diagnosis of ulcer had been made early, before the ulcer had made inroads into the stomach, what could have been done for the patient? In view of the findings at the present time, it seems as though the case would have been hopeless from the beginning, but is it not possible that other cases might be operable? The use of Sauerbach's operative cabinet has been of advantage in operating on cases of carcinoma of the esophagus, and it seems to me that it might be of advantage in such cases as this. If, however, no operation would have been possible, the early use of esophageal dilators might have kept the contraction of the esophagus down and permitted the nourishment of the patient until the ulcers could have been healed.

I am indebted to Dr. Johnson, second assistant pathologist, for the pathologic report of this case.

CEREBRAL HEMORRHAGE: LUMBAR PUNCTURE

CASE II.—T. S., male, German, aged 43 years, a milk dealer. His family history was negative. He had always been well until three years ago, when he began to have attacks of headache, occurring every two or three days, accompanied by vertigo. He denies venereal infection. He has always been a hard worker and has been a free user of alcoholics since a boy. In late years he has drunk as much as twenty glasses of wine or whiskey a day. His appetite has been poor for several years. His bowels have been regular. Frequently he has had nocturnal involuntary urination.

At 5.30 P.M., January 18, 1905, while eating supper, the patient's right hand and arm began to tremble, and he complained

of the arm feeling peculiar, and almost immediately fell from the chair to the floor. His body was relaxed and no convulsions were present; the patient was conscious, but when he attempted to answer questions he could not speak so that his friends could understand him. On attempting to stand it was found that his right leg and right arm were paralyzed. The patient was placed in bed and slept at intervals during the night. On the morning of the 19th, at 8 o'clock, he was seized with a convulsion, which was bilateral, the entire body trembling and shaking violently, the head turning toward the left and the eyes oscillating, and some frothy sputum exuding from the mouth. The patient's wife stated that "his cheeks blew out when he breathed."

The patient entered the Presbyterian Hospital at 10 A.M. January 19. He had seven convulsions that morning, each convulsion lasting about two minutes, and occurring at intervals of fifteen to twenty minutes. The patient was a large, well-formed, but sparsely nourished man, weighing about 180 pounds. He was in deep coma, breathing stertorously, and the left cheek protruding more than the right. Examination of the organs was negative, except the liver, which was slightly enlarged. The legs were perfectly relaxed, the reflexes being almost absent; the abdominal and cremasteric reflexes were absent on the right side. The pulse was rapid, 144, full and regular; the systolic blood-pressure was 190; the diastolic, 188. The respirations were 40 per minute, and the temperature 101° F. Blood examination revealed 3,500,000 red cells, 13,600 white cells, and 70 per cent. of hemoglobin. The urine, removed by catheter, was clear, straw-colored; specific gravity, 1027; it contained considerable albumin, all kinds of casts, epithelial cells, red and white corpuscles, and a large percentage of sugar. Dr. Tieken made a cryoscopic examination, with the following results:

Blood, first examination, freezes at -0.62° C.

Blood, soon after transfusion, freezes at -0.59° C.

Cerebro-spinal fluid freezes at -0.64° C.

Blood, second examination, freezes at -0.72° C.

Cerebro-spinal fluid, second examination, freezes at -0.64° C.

Urine, catheterized, freezes at -0.68° C.

The first examination was made soon after the patient's arrival at the hospital; the second immediately after the transfusion of

1000 c.c. of salt solution; the third, at the second venesection; and the spinal fluid was frozen immediately after the puncture was made.

The clinical features of the case, in the absence of a detailed history of the case, gave rise to a nice opportunity for differential diagnosis. The question arose, What is the exact condition present—alcoholism, uremia, or cerebral hemorrhage? In favor of alcoholism was the history of the patient. In favor of uremia were the urinary findings, the convulsions, and the concentration of the blood and urine, as found by cryoscopy. In favor of cerebral hemorrhage was the hemiplegia. It was again considered that the patient might be, and probably was, suffering from a combination of these conditions. But, in any event, it was decided that the treatment for uremia should be instituted. Accordingly, 500 c.c. of blood was withdrawn from the left arm, and 1000 c.c. of normal saline solution was given. Thirty grains (2 grams) of chloral was given by the rectum, and $\frac{1}{4}$ grain (0.015 gram) of morphin hypodermically, to control the convulsions; but without avail. Chloroform was also tried for this purpose, without success. Then a lumbar puncture was made, and 35 c.c. of spinal fluid was withdrawn, after which the patient had no more convulsions, having had twelve up to this period. Near midnight of the 19th the patient began to move his left arm and leg, and on the following morning was quite rational. The next night (20th) he became delirious, the delirium simulating delirium tremens. The following morning he again became comatose, and a second lumbar puncture was made, and within five minutes the patient came out of the comatose condition and passed into a state of low muttering delirium. Five hundred c.c. of blood was again withdrawn, and pilocarpin was given hypodermically. But the patient's temperature began to rise, until it reached 106.4° F., and he died on the night of January 22, three days after entrance into the hospital.

An autopsy was made immediately by the assistant pathologist, Dr. Peter Bassoe, with the following results:

The body is that of a well-developed, but sparsely nourished man. There is slight posterior lividity; no edema. Peritoneal cavity: No fluid; fibrous adhesions about spleen. Lungs: Left: Upper lobe crepitates perfectly. Lower lobe: Cut surface is grayish-red, rather dry, and less crepitant than upper. Mucopus comes from bronchi

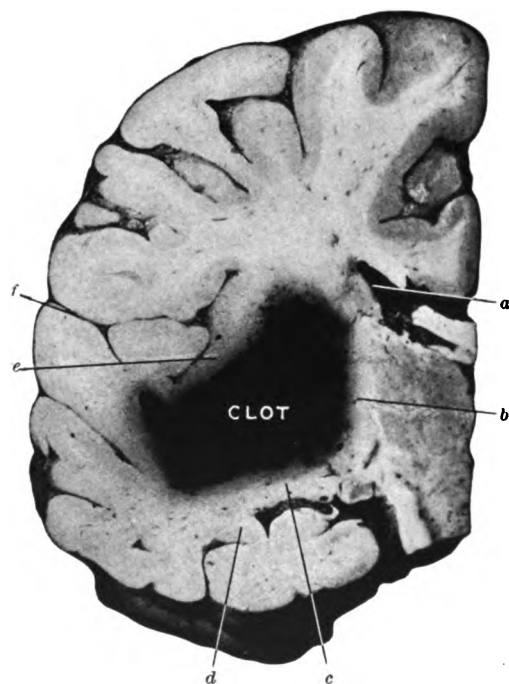


FIG. 2.—Hemorrhage into the left corpus striatum. *a.* Lateral ventricle; *b.* thalamus; *c.* hippocampus; *d.* descending horn; *e.* island of Reil; *f.* Sylvian fissure.

of lower lobe, and the tissue is somewhat friable. Weight: 530 grams. Right: Upper and middle lobes quite spongy, resembling left upper; lower lobe answers to description of left lower. Weight: 450 grams. HEART: Epicardium smooth; endocardium and valves smooth; foramen ovale closed, except for a very small opening at margin. Left ventricular wall is 1.5 to 2 centimeters thick, and the ventricular cavity is 8 centimeters long. The right cavity is same length. Numerous, almost continuous, raised, yellowish-white areas in coronary arteries. Myocardium firm and of uniform color. Thoracic aorta: Comparatively few raised whitish areas. Spleen normal. Stomach of normal size; lining smooth, with prominent rugae, which do not obliterate on stretching. Mucosa hyperemic in places, and coated with small amount of mucus. No marked changes in intestines. LIVER: Weight, 1800 grams. Cuts with slightly increased resistance; surface, grayish-red; lobular markings rather indistinct. KIDNEYS: Weight together, 300 grams; equal size. Left: Capsule peels readily, leaving a surface which is divided into small elevated areas, with furrows which run in all directions. Near one pole there is a distinct sunken area in the convexity. Cut surface, mottled, grayish, and dark red in color, and considerable blood can be expressed. Cortex, 8 to 10 millimeters thick; markings rather obscure, though they can be made out in most places. Pyramids resemble the cortex in color. Pelvis smooth. BRAIN: Weight, 1170 grams. Pia over both sides of cortex is raised and edematous; cortex sunken. Lateral ventricles contain clear fluid. Internal carotid arteries dilated. Basilar artery smooth. Recent hemorrhage into left corpus striatum (Fig. 2).

ANATOMIC DIAGNOSIS.—Chronic interstitial nephritis; general moderate arteriosclerosis; hypertrophy of the left cardiac ventricle; atrophy of the brain, with recent hemorrhage into the left corpus striatum; hypostatic bronchopneumonia of both lower lobes; fatty liver; chronic catarrhal gastritis and hyperemic colon.

HISTOLOGIC EXAMINATION.—Lung: Sections show typical bronchopneumonia. Liver: Fatty change and passive congestion. Spleen: Trabeculae abnormally large and numerous. Kidneys: Marked passive congestion, considerable increase in connective tissue, with irregular areas of round-cell infiltration. Many of the Malpighian corpuscles are obliterated and replaced by connective tissue, which in many places extends to the surface where the cap-

sule is thickened and sunken. Bowman's capsule in many places is greatly thickened; there is also a great increase of connective tissue.

In this case, as in many others, the great diagnostician, the pathologist, cleared up the cloudy points, but a review of the clinical findings, and the result of the lumbar punctures, presents a picture which is interesting, if not instructive. If the urinary findings alone established the fact that nephritis was present, it would not be sufficient for us to insist that the convulsions were the result of the nephritis, but when the blood and urine are so concentrated, as found by cryoscopic examination, the ground that the condition was probably uremic would be well taken. Of course, the cerebral hemorrhage would cause symptoms which might overshadow any uremic symptoms, or which would further complicate the diagnosis, but it would be difficult to separate the two conditions. But an interesting fact was the prompt relief which lumbar puncture gave the patient for a short time. The removal of the spinal fluid relieved the intracerebral pressure, and the irritative convulsions ceased, just as they do so frequently in cerebrospinal meningitis.

NON-RENAL CURABLE ALBUMINURIA

The presence of albumin in the urine is generally considered evidence of disease of the kidneys, and if found in life insurance examinations the applicant for insurance is generally rejected, and he is informed that he is the subject of serious disease. In the majority of instances the urine of such subjects does not contain the microscopic evidence of organic disease of the kidneys, and the researches of Councilman and Cabot have proved that even when the urine contains casts, and the clinical diagnosis of nephritis is made, the post-mortem findings do not always corroborate the diagnosis. During the past few years I have had several cases of accidental albuminuria which cleared up under treatment, and the patients were relieved from the dread of serious disease being present. Accidental albuminuria may be the result of various causes. It is frequently found in individuals who are intense mental laborers of sedentary habits. For example, one of my patients was a business man, about 40 years of age, spare of body and intensely nervous, wiry, and an indefatigable worker; a man who was at the head of three large manufacturing establishments; a member of the board of one of our large municipal bodies, and who was not

satisfied with dictating to a stenographer at his places of business, but had a stenographer at his residence and dictated to her after his return home late in the evening. He desired a large life insurance, and, as was to be expected, was rejected because of albuminuria. No evidence of disease of the urinary tract was found. He was advised to change his mode of life, and was warned that he was burning the candle at both ends. The result was that the change caused a complete disappearance of the albuminuria, and the subsequent admission to the insurance company.

A second example was a young man, aged 24 years, a school-teacher, who was refused life insurance on account of albuminuria. The urine was albuminous, but contained no casts. Catheterization of the ureters proved the fact that the urine from both kidneys was albuminous. There was no history of previous venereal infection, or evidence of disease of the bladder. He was placed on strict dietetic and hygienic regime, and during the summer by advice took a trip down the Mississippi River on a house-boat from St. Paul to St. Louis, securing rest and outdoor life. On his return his albuminuria had completely disappeared, and he has remained in perfect health since.

The third case was a man, 40 years of age, of sedentary habits and of nervous temperament, but in a business which involved a great deal of worry. He denied previous venereal infection, but he had been exposed to such infection a great many times, and there was present catarrhal cystitis, which evidently had been of long standing. Catheterization of the ureters proved the fact that the albumin was from the kidneys. There were no casts. The cystoscope revealed quite an extensive catarrh at the base of the bladder. The patient underwent a course of treatment of bladder washing, with the instillation of silver nitrate and the filling of the bladder with a 10 per cent. solution of protargol. After several months' treatment the albuminuria disappeared permanently.

These cases illustrate the fact that accidental albuminuria may result from excessive metabolic and katabolic changes, especially in brain workers, or that it may come from the renal pelvis, the ureters, the bladder, or the urethra, or through an abnormal communication from the neighboring parts, such as the lymphatics or thoracic duct. The differential diagnosis may generally be made by a careful chemical and microscopic examination and the use fre-

quently of the urethral catheter. We can exclude organic disease if casts are absent, and many times when they are present. The physical examination is more important than the urine analysis. The sufficiency of the kidneys, and the weight of the urine and the solids that are excreted, are of value in diagnosis. Is there dropsy? What are the eye findings? What is the state of the heart and of the arterioles? The blood-pressure? And what does cryoscopy teach us?

The fact that many cases of albuminuria, which were regarded as hopeless and which frequently recovered, had been observed by many observers, should caution us to be extremely guarded against condemning a patient to a life of worry by an unfavorable prognosis.

ADDISON'S DISEASE

A CLINICAL LECTURE DELIVERED AT THE COOK COUNTY HOSPITAL, CHICAGO

BY EDWARD F. WELLS, M.D.

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GENTLEMEN: More than once I have had occasion to call your attention to the fact that this hospital furnishes for your instruction not only cases illustrating the ordinary diseases which you will encounter in general practice, but examples of the rarer morbid conditions as well. Some of these cases will now engage our attention.

Clinical medicine is largely concerned with diagnosis, prognosis, and treatment, and I can assure you that there is no satisfactory success as a physician attainable without conspicuous superiority in these fields. They are fundamental branches of the art of medicine, and, as in all arts, the conspicuous superiority of which I spoke, can only be obtained by those who are willing to study these subjects at first hand by long and patient observation of the living patient and the dead subject. In addition, there is required an inherent capacity for broadly and in proper perspective seeing and doing things. In its simplest form diagnosis may be very easy indeed, even in uncommon affections, as is illustrated by our first case:

This woman, youthful-looking for her 73 years, as you may see at a glance, presents small spots of brown pigmentation over all the visible portions of the body. About the eyes, in front of the ears, around the mouth and, especially, upon the neck, there are large patches of darker discoloration. The lips and the palpebral margins are very dark. Below the left clavicle, where the collar has become loosened, there are a number of white spots scattered over the dark field. You instantly make the nosologic diagnosis. It is Addison's disease. In no other malady will you find the appearances here presented. In all cases, however, more than a name is required to

complete your diagnosis; it is necessary that you estimate the degree and character of the affection, and certainly this should not be neglected in one so interesting as this promises to be.

There is nothing in the family or personal history of this patient which can have any bearing upon her disease; she never received any injury of the back or abdomen; there have been no symptoms which point toward tuberculosis. In this case, as is usual, the onset of the malady was so insidious that the patient cannot tell when it began. She states that her health had always been good until 5 months ago, at which time gradually increasing weakness and brownish pigmentation attracted her attention. Since then there have been: Increasing muscular weakness, until it is now profound; mental asthenia, now apathy; a drowsy state, advancing to the point that she desires to sleep nearly all the time, although she awakens easily and completely; dizziness and a tendency to fainting upon turning in bed or on assuming the erect position; a moderate desire for food, but too much weariness to take it; a spreading and deepening of the peculiar brownish discoloration of the skin, with the appearance of leukodermatous patches. Each of these features have advanced to a degree that, as you can readily see, may be fairly described as profound.

Of pertinent negative symptoms we may mention: There have been no pains in the back; no nausea nor vomiting; no diarrhea; no marked diminution of the subcutaneous fat; no great discomfort.

Let us now closely examine this patient: The peculiar and typical discoloration first attracts our attention. With the excellent light you may see these small spots of brown pigment covering the entire body—the face, chest, abdomen, back, and limbs. Everywhere they are closely massed, and in many places they form large patches of nearly solid color. These patches are especially noticeable upon the neck, in the axillæ, in the groins and joint flexures, around the orifices, etc., and at these places they are so dark as to be almost black. The lips and margins of the eyelids are, as you may plainly see, quite black. The matrices of the nails are markedly pigmented, and to this I call your attention because it is an unusual feature. I will also ask you to note, particularly, that, beginning 2 or 3 inches above the ankles and extending over the ankles and parts of the feet, the color is much darker than over other portions of the legs; that above the knees the thighs are encircled by dark bands about 2

inches wide; that a broad dark stripe extends down the abdomen from the ensiform cartilage to a couple of inches above the pubis. Upon inquiry you hear her inform us that, up to a week ago, she had persisted in wearing corsets with heavy front stays; high shoes tightly laced about the ankles, and, you saw, when the nurse removed the patient's stockings, that they were supported by broad elastic garters above the knees. These are especially interesting coincidences, because it is well known that in Addison's disease pressure upon or injury to the skin produces such discolored patches. You see, when the inside of the patient's mouth is exposed, that the mucous membrane is also discolored, numerous pigmented spots being scattered over the roof of the mouth, the pendulous soft palate, and especially broad and irregular stripes on both sides running from the labial fissure to the angle of the jaw. She has only two teeth, but where these impinge the mucous membrane shows a dark spot. You will note that when I prick the mucous membrane at any point within the mouth the patient manifests no signs of pain; sensation is absent. A blood count shows, hemoglobin, 37 per cent.; red corpuscles, 3,200,000; leukocytes, 7200, the lymphocytes being in excess.

I have intentionally omitted mention until this time, notwithstanding the broad endeavors of some of you to call my attention to the patent fact, of the second of the two most striking features of this most interesting case. I refer to the remarkable display of white spots and patches scattered through the brown areas. They are most numerous and conspicuous upon the back and chest, but are found elsewhere as well. If you will examine them closely you may notice that they vary in size and degrees of whiteness; everywhere there are minute white spots; upon the back and chest there are a number of patches of large or considerable size. Some of these are merely, and clearly, a lightening of the brown pigmentation; others are cream-colored, and a great many are very white. Here also you notice that when I prick the skin there is everywhere a diminution, and in the vitiligenous spots an absence, of sensation. I noticed that some of you were impressed, as I was myself when I first noticed it, by the white streaks to be seen in both the buccal stripes, and the white spot in one of the brown patches where the teeth press against the mucous membrane of the mouth.

Of the pertinent negative findings these may be mentioned: The

pulse is not unduly frequent, and is of better tension than one might reasonably expect; the respiration and temperature are normal; the urine is not abnormal; there are no cardiac murmurs; the general appearance of the patient is fairly good.

Now, gentlemen, although there are other symptoms and findings, I believe that we have presented every feature which has an important bearing upon this case, and we may profitably compare it with others which I have observed in this hospital and elsewhere, or have been reported in the literature.

You already know that, although cases which we now class as examples of this malady were reported by Lobstein in 1823, by Schotte in the same year, by Bright in 1829, and possibly by others, yet to Addison, who published his work in 1855, is due the credit of firmly placing the disease which bears his name in the catalogue of special maladies. His description of this clinical entity is so elegant that it will bear repetition at this time:

"The leading and characteristic features of the morbid state to which I would direct attention are—anemia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of color of the skin, occurring in connection with a diseased condition of the supra-renal capsules.

"As has been observed in other forms of anemic disease, this singular disorder usually commences in such a manner that the individual has considerable difficulty in assigning the number of weeks, or even months, that have elapsed since he first experienced indications of failing health and strength; the rapidity, however, with which the morbid change takes place varies in different instances.

"In some cases that rapidity is very great, a few weeks proving sufficient to break up the powers of the constitution, or even to destroy life, the result, I believe, being determined by the extent, and by the more or less speedy development of the organic lesion.

"The patient in most of the cases I have seen has been observed gradually to fall off in general health; he becomes languid and weak, indisposed to either bodily or mental exertion; the appetite is impaired or entirely lost; the whites of the eyes become pearly; the pulse small and feeble, or perhaps somewhat large, but excessively soft and compressible; the body wastes, without, however, presenting the dry and shrivelled skin and extreme emaciation usually attendant upon protracted malignant disease; slight pain and uneasi-

ness is from time to time referred to the region of the stomach, and there is occasionally actual vomiting, which in one instance was both urgent and distressing; and it is by no means uncommon for the patient to manifest indications of disturbed cerebral circulation.

"Notwithstanding these unequivocal signs of feeble circulation, anemia, and general prostration, neither the most diligent inquiry nor the most careful physical examination tend to throw the slightest gleam of light upon the precise nature of the patient's malady; nor do we succeed in fixing upon any special lesion as the cause of this gradual and extraordinary constitutional change.

"We may, indeed, suspect some malignant or strumous disease—we may be led to inquire into the condition of the so-called blood-making organs—but we discover no positive proof of organic change anywhere—no enlargement of the spleen, thyroid, thymus, or lymphatic glands—no evidence of renal disease, of purpura, of previous exhausting diarrhea, or ague, or any long-continued exposure to miasmatic influences; but with a greater or less manifestation of the symptoms already enumerated, we discover a most remarkable and, so far as I know, characteristic discoloration taking place in the skin—sufficiently marked, indeed, as generally to have attracted the attention of the patient himself or of the patient's friends.

"This discoloration pervades the whole surface of the body, but is most strongly manifested on the face, neck, superior extremities, penis, and scrotum, and in the flexures of the axillæ and around the navel.

"It may be said to present a dingy or smoky appearance, or various tints or shades of deep amber or chestnut-brown; and in one instance the skin was so universally and so deeply darkened, that but for the features the patient might have been mistaken for a mulatto.

"This singular discoloration usually increases with the advance of the disease; the anemia, languor, failure of appetite, and feebleness of the heart, become aggravated; a darkish streak usually appears on the commissure of the lips; the body wastes, but without the emaciation and dry, harsh condition of the surface, so commonly observed in ordinary malignant diseases; the pulse becomes smaller and weaker; and, without any special complaint of pain or uneasiness, the patient at length gradually sinks and expires."

The brown pigmentation is the symptom which usually first attracts attention, and it is strange that this is, usually, so far

advanced before it is noticed by the patient or his friends. In this patient it was nearly as prominent as you now observe it.

I remember my first case of this disease, as if it were but yesterday: A middle-aged man consulted me in alarm because, as he asserted, his penis had turned black over night. As a matter of fact, the condition had simply suddenly attracted his attention. Upon inquiry I learned that a physician whom he had consulted several months previously had asked him if he had ever taken nitrate of silver for any length of time, offering in explanation for the query that persons who long take the medicine have their skins discolored, but not exactly as was the face of the patient. Certainly it was a fact that he showed the characteristic pigmentation markedly in the usual situations, with many spots and patches of leukoderma.

Whether the discoloration or the asthenia take precedence in the order of events, or whether they develop simultaneously is not certainly known, and but few observations upon this point have been made. In one case, in my service in this hospital, the pigmentation followed the anemia and prostration:

A man, aged 53 years, was admitted for anemia and general debility. He complained of weakness, pain in the back, nausea and vomiting, dizziness and mental dulness. He was decidedly anemic. There was no evidence of nephritis, nor of pernicious anemia. Notwithstanding his weakness, poor appetite and attacks of vomiting, his weight was fairly well maintained. After he had been in the hospital for a few weeks it was noted that his face and neck were discolored, and examination showed very considerable advances in the ordinary situations for these deposits. Later, under our observation, the leukodermatous patches made their appearance. In this case the numbness and sensory paresis of the mucous membranes of the mouth were marked, as was also the anesthesia of the vitiligenous patches. Very careful thermometric observations were made for several weeks, the temperature being always below normal. Tuberculin was used, for diagnostic purposes, with negative results.

You noted particularly, in our patient of to-day, the large dark patches at places where pressure had long been made, as, for example, by the shoetops around the ankles; by the garters above the knees; by the corsets down the front of the abdomen; by the teeth in the mouth. This intensification of the pigmentation from irritation, as from pressure, friction, a blister, etc., has long been known,

and in doubtful cases the fact may be employed for diagnostic assistance. In this connection I wish to caution you not to consider every case in which discoloration follows surface irritation or injury as one of Addison's disease, inasmuch as such discolorations are not uncommon as a temporary sequence in healthy persons. However, taken in connection with other symptoms and signs, it may be of material diagnostic aid.

In this case the vitiliginous spots and patches are peculiarly prominent. These have been present, to the best of my recollection, in every case which I have seen. They were present in each of the 4 cases which have been treated in this hospital during the last few months. If you consult the literature upon this subject the statement which I have made will be a matter of surprise, as the fact long was to me. It is indeed remarkable in how many cases these white spots can be looked at by patients, laymen, and some physicians, without their being recognized; and in this, after you have seen a number of patients of this kind, I am quite sure you will agree with me. I have no hesitation in asserting that these leukodermatous spots are present in a very much larger proportion of patients than a survey of the literature would lead you to expect.

It is of historical interest to note that one of Addison's original cases was marked by this peculiar leukoderma. His observations were made in Guy's Hospital. Wilkes and Greenhow were young men in this institution at that time, and they, especially Wilkes, furnished the case histories for Addison's book. They were deeply interested in the inquiry, continued their investigations, and made important subsequent contributions to the subject. Not long after Addison's publication Wilkes reported a number of additional cases, from which he argued, with much color, that Addison's disease was a malady *sui generis*, having a peculiar clinical history and a special morbid anatomy; namely, a general asthenia and bronzing of the skin, associated with tubercular destruction of the suprarenal capsules. Now it so happened that Addison's case, in which vitiligo was present, was not submitted to autopsy, and that all of the cases reported by Wilkes were free from this symptom. From these facts Wilkes argued that Addison's vitiliginous case, and others of the same kind, were not examples of true Addison's disease. In this matter, however, I can assure you that our distinguished pioneer was mistaken.

Languor and debility are always present. The patient is tired; he is disinclined to move; if he exerts himself he quickly becomes fatigued; apathy develops; he becomes too indifferent and tired to eat and drink; exhaustion and profound prostration ensue. It is true that, generally, these symptoms creep along almost unnoticed, yet I have seen patients maintain a fair degree of strength and activity until the discoloration had assumed advanced appearances, with, then, a sudden decline and death in a short time.

You remember that our patient has had no marked digestive disturbances, although these are present, as a rule. They show themselves as a sense of fulness after eating, with, later, nausea and vomiting, and, often, with a foul diarrhea. Epigastric pain, sometimes intense, and with tenderness, is often present. In some cases the slightest touch upon the abdomen produces nausea, a cold sweat, or faintness. Lumbar and sacral pains are common.

The duration of the disease, dating from the time symptoms are first noticed, varies from a few weeks to several years, with an average of about two years. You may encounter, very rarely, cases in the young which run their course in so short a time that they may be fairly called acute. In these sudden death is not infrequent. In others the duration may be greatly prolonged. I have a patient under observation in whom the disease has existed at least 15 years. Rapid advance, retardation and temporary improvement alternate in periods of varying length. Notwithstanding the few cases in which a cure is said to have occurred, it may be stated that Addison's disease is one terminating in death.

The diagnosis in the case before you is clear, both as to clinical history and objective appearances. In typical and advanced cases you will have no difficulty in making a diagnosis, but the early and atypical ones may require, at your hands, the nicest analysis of the presented facts before a conclusion can be reached.

The active secretion of the suprarenal glands necessarily enters the circulation and should be found in the blood and extra-vascular serum. May we not anticipate the near future, when some one of you, perhaps, will furnish us with clinically available tests by which we may demonstrate in these fluids the presence, or absence, of this substance, thereby placing the diagnosis of Addison's disease upon a firm scientific footing?

Without going fully into the evident reasons therefor, you will

understand that this malady must be differentiated from some unusual cases of vagabond's disease, pelagra, cancer, tuberculosis, Graves's disease, pregnancy, ovarian tumor, diabetes, jaundice, arsenical and argentic discolorations, and various unclassified pigmentations; but with reasonable care mistakes will rarely be made.

What shall we do, gentlemen, to relieve or cure our patient? This is one of the diseases in which specific treatment, by supplying the system with a lacking, but vitally necessary secretion, should be useful and curative. Attempts upon a large scale have been made, but with only indifferent success. These unsatisfactory and disappointing results are probably due to the fact that we have not, as yet, been supplied with the required substance in proper form, or our methods of administration have been defective. As the matter now stands, we should give, in every reasonable manner, suprarenal glands (raw, cooked, or desiccated) from domestic animals; or the probably active principle in the form of adrenalin, suprarenin, etc., with the assurance that the underlying principles of our treatment is correct, and that success will almost certainly attend the perfection of our details. During recent years my own patients have been given 10 to 15 drops of the 0.1 per cent. solution of adrenalin chlorid, diluted in 3 to 6 ounces of water, 3 or 4 times a day, after eating.

The implantation of portions of suprarenal glands has not been attended with success, and probably but little can be expected in this direction. However, experiments along these lines should be continued.

In the practical management of these cases you will be largely dependent upon symptomatic treatment: The patient should be allowed, or given, more rest than seems necessary; and when vertigo or syncope are marked symptoms he should be kept in the recumbent position, and not be permitted to rise suddenly, nor to make straining efforts. You should carefully supervise the diet, in order that the patient receive sufficient foods and drinks of proper quality, and that unsuitable foods, and those which disagree, may be interdicted. If there are evidences of intestinal fermentation, as often occurs, some efficient intestinal antiseptic should be used. In the management of the persistent vomiting which is encountered in some of these cases you will obtain the best results from the temporary withdrawal of all foods, or the giving of only the blandest of these; the

use of hot water at frequent intervals; the giving of minute doses of cocain hydrochlorate, $\frac{1}{16}$ to $\frac{1}{32}$ grain (0.00025 to 0.0005 gram), frequently repeated, being careful that the total amount given is not sufficient to cause depression; by making stimulating applications to the spine and over the abdomen; by the cautious use, hypodermically of minute doses of morphin, $\frac{1}{8}$ to $\frac{1}{4}$ grain (0.004 to 0.005 gram); the use of a stimulating enema, such as, glycerin 2 ounces (60 c.c.), magnesium sulphate 2 ounces (60 grams), and water 12 ounces (360 c.c.). Should diarrhea supervene, it should be accorded the most careful consideration: The patient should be placed at once upon a milk diet, and one of the tannin preparations given in small and frequently repeated doses. Stimulants will probably be required, as will also the external application of heat. In those cases in which life is imminently threatened by collapse you should have recourse to hypodermoclysis of normal salt solution.

Let me warn you against the indiscriminate use of cathartics in Addison's disease. They should be employed with the greatest caution, as they have been the immediate cause of death in a number of cases.

Digitalis, by the mouth in the blandest forms if it can be borne, or hypodermically, should be used to give tone to the paretic vessels and heart. In my cases the patients receive from 5 to 10 minims (0.3 to 0.6 c.c.) of a reliable tincture, or an equivalent dose of the infusion of digitalis 3 times a day, after meals, continuously or with intermissions, for months. In my experience it has always been well borne, except at the time of the gastric crisis, and I have not felt that these have been precipitated.

At the end your patient dies, and it is interesting and important for you to know the morbid anatomy which will be found, inasmuch as by it you will obtain valuable information bearing upon the pathogenesis, prognosis, and treatment of this peculiar malady. I here show you the involved organs obtained from a patient observed in my service in this hospital about 2 years ago:

The patient was a male, of middle age, in whom the clinical history and objective findings were ordinary and quite typical. He entered in a profoundly prostrated state and died in a few days. At the autopsy the following pertinent findings were noted: There was a fairly symmetrical enlargement of both suprarenal glands. They were irregularly nodulated, of increased resistance and adherent by

radiating extra-capsular fibrous septa in the surrounding areolar tissue for very considerable distances, so that extensive areas on both sides were involved in a firm fibrous grasp. In this were implicated the sheathes of blood-vessels and nerves, together with their ganglia. On section the glands were found in a very peculiar condition. There was such extensive caseation, with cheesy and calcareous deposits, lying between bands and masses of fibrous tissue that practically no normal glandular tissue remained. The cut surface was mottled and the cortical and medullary portions of the gland could not be differentiated. Tubercle bacilli could not be obtained. The subcutaneous fat was abundant. You may see almost all of these features in the specimens which are being passed around.

In general, this is the condition found post-mortem. Exceptions to the rule lie in the cases which have been reported in which other conditions of the gland have been found, as, for instance, absence or marked hypoplasia of the organs; simple atrophy; inflammatory states; interstitial hemorrhages; new growths; the normal state. I am convinced, however, that these cases should be subjected to further critical analysis before they shall be admitted to the permanent literature of the subject.

Before applying the facts of morbid anatomy to the pathogenesis of Addison's disease it may be well for us to review, very shortly, the normal anatomy and physiology of the suprarenal glands:

The suprarenal glands, discovered by Eustachius in 1564, are two small but vitally essential glands unsymmetrically situated in close proximity to, but independent of, the upper end of the kidneys. Each weighs from 50 to 100 grains, being relatively larger in children and smaller in the aged. They are very abundantly supplied with blood-vessels and nerves. The glands consist of medullary and cortical portions, well supported by fibrous septa, which are continuous with the capsule. They are rarely displaced, and do not participate in renal dislocations. Accessory glandular fragments are found in most persons at the hilum, between the bodies and the genital glands, and elsewhere. Congenital aplasia and hypoplasia have been observed, especially in connection with cerebral defects. The glands secrete a substance (variously termed suprarenin, adrenalin, etc.) which is essential to the proper maintenance of blood-pressure. This substance may be extracted from the glands and is in common use for therapeutic and experimental purposes, causing

when locally applied extreme contraction of the capillaries, and when introduced into the veins increase in the arterial tension. It is very susceptible to oxidation, by which its color is changed to pink and its activity impaired.

From all the facts which I have placed before you, together with others which are relevant, but which you can best obtain from your text-books, we may fairly infer that Addison's disease is due to great diminution or absence of the peculiar and vitally necessary secretion of the suprarenal glands, to which detailed reference has been made. We know that such secretion exists, and we also know that in the malady under discussion the suprarenal glands are destructively affected. It is true that these glands have been found destroyed in some cases in which the symptoms and signs of Addison's disease did not appear; but in explanation of these it may be assumed that accessory glands were present, by which sufficient secretion was furnished the system, or that the disease was present in a mild and unrecognized form. In this connection, however, I must point out that recently Wiesel¹ has published the results of certain very interesting and important studies of the chromaffin system and its relation to the pathogenesis of Addison's disease. He suggests that Addison's disease is a specific affection of the chromaffin cells of the body, especially of the suprarenal medulla.

In conclusion, let me urge you to study these cases carefully from the scientific side, but in this do not fail to apply all the arts of medicine in attempting to alleviate distressing symptoms and to prolong life.

¹ The Anatomy, Physiology, and Pathology of the Chromaffin System, with Special Reference to Addison's Disease and Status Thymicus, *INTERNATIONAL CLINICS*, 15th Series, 1905, ii, 288.

A CASE OF CHRONIC JAUNDICE AND GREAT ENLARGEMENT OF THE LIVER, DUE TO PRIMARY CARCINOMA OF THE EXTRAHEPATIC BILE DUCTS, COMMENCING AT THE JUNCTION OF THE HEPATIC DUCTS

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AND

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THE patient, George W., aged 35 years, was admitted to the German Hospital, July 24, 1904, for deep jaundice and enlarged liver. The jaundice commenced early in July, without pain or any gastric disturbance. Dr. Leonard Williams, who saw the man in the Out-Patient Department two weeks or so before his admission, says that at first the liver appeared not to be enlarged. There was no history of gall-stones or previous jaundice, and the general health was said to have been good. There was no evidence of syphilis, alcoholism, or hereditary tendency to disease of the liver.

On admission the jaundice was extremely deep. The liver was greatly and uniformly enlarged, extending downward on the right side of the abdomen to the anterior superior spine of the ilium. It seemed hard, and its surface was smooth. The spleen was also somewhat, but not greatly, enlarged. The feces were invariably colorless, and the urine deep brown from the presence of bile. It was free from sugar and practically free from albumin, but, as in most cases of deep chronic jaundice, it showed a marked "cloud" of nucleo-albumin on adding acetic acid, either in the cold or after boiling. It likewise contained the usual golden orange pigmented cells, and a few hyaline tube casts, as urines of severe jaundice always do.¹

¹ It is perhaps only in the most extreme degrees of jaundice, with chronic obstruction in the common bile duct, that the urine gives the very marked reaction for a mucinoid substance, or nucleo-albumin, to which one of us alluded in *Trans. Path. Soc., London, 1900, vol. li, p. 176*. On the other hand, in all, or nearly all, cases of jaundice with complete obstruction to the escape of bile (even when of relatively short duration), casts can be found in the urine,

Apart from the jaundice, the patient seemed to be in fairly good health. There was never any xanthoma, practically no prurigo, and no bleeding from the gums or tendency to cutaneous hemorrhages. The only peculiarity, apart from the disease for which he was admitted, was the very tall or "turriform" shape of his head (German, "Turmschädel"), which, however, has no bearing upon the subject of our paper. Nothing abnormal was noted in the thoracic organs. There was no enlargement of any of the accessible lymphatic glands. Examination of the blood (September, 1904) gave the hemoglobin value as 80 per cent. of the normal. The red cells were 3,880,000 in the cubic millimeter, and the white cells 7000.

Owing to the possibility of the obstruction to the outflow of bile being due to a syphilitic lesion at the hilum of the liver, prolonged treatment by potassium iodid was tried, but with no obvious result. Olive oil given by the mouth likewise had no effect.

On October 7, 1904, Dr. Michels performed an exploratory laparotomy, with the object of discovering the cause of the biliary obstruction, and remedying it if possible. At the operation the liver was found very large and rather hard; it had a dark, congested appearance; its surface was not granular. No biliary calculus was felt after full exposure of the bile ducts, nor could Dr. Michels make out any swelling or tumor in the pancreas, or at the hilum of the liver, which might be compressing the extrahepatic bile ducts. There were no adhesions about the gall-bladder, which was small, not much distended, and so far behind the edge of the liver that cholecystostomy could not have been safely undertaken, even had it

if carefully searched for, though albumin be absent. These casts may contain pigment granules and pigmented cells. Nothnagel (*Deut. Arch. für klin. Medicin*, 1874, vol. xii, p. 326) thought that in every marked case of jaundice, whatever the cause of the jaundice, casts appear in the urine. (Cf. Dr. P. S. Wallerstein, *Ueber reine Cylindrurie bei künstlich erzeugter Gallenstauung*, *Berliner klin. Wochenschrift*, 1902, No. 14, p. 310.) Zeri (*Il Morgagni*, October, 1904), from observations of 30 cases of jaundice, concluded that renal epithelial cells and casts formed from degenerated renal epithelium could frequently be found in bilious urine, even in the absence of albumin. He thought that the epithelial cells and casts in the urine of icteric patients signified damage to the renal tubules, whilst albuminuria, when it occurred in such cases, pointed to damage of the glomeruli. In the present case we were able to note the disappearance (except for the ordinary faint trace) of the nucleo-albumin from the urine when the biliary retention was relieved. It is possible that the nucleo-albumin of bilious urines may, like the bile-pigments, be derived from the bile-passages.

been otherwise desired. Neither the common bile duct, nor any of the bile ducts which could be felt and seen outside the liver were distended.

The patient did not appear to suffer from the operation, though for a time the jaundice seemed still more intense. The wound healed fairly rapidly, and he was soon able to get about again. The jaundice and his general condition were apparently about the same on November 5, 1904, when he left the hospital, as they were on admission.

He was readmitted on November 24, 1904, with the idea that an operation might be performed to drain off the bile externally. The complete and constant absence of bile from the bowel and the history of the case made it practically certain that the condition of the liver was due not to a form of Hanot's cirrhosis nor to any form of cholelithiasis, but that it was caused by complete obstruction in the large bile ducts from a cause which could not be ascertained at the exploratory operation, in spite of careful examination of the region of the transverse fissure. (The result showed that the tumor causing the jaundice must at the time of the first operation have been very small and situated deep in the transverse fissure at the junction of the two hepatic ducts.) It was finally decided, after consultation with Dr. zum Busch, to establish a biliary fistula by the method suggested by M. Hirschberg² and J. Rotter.³

This operation was performed by Dr. Michels on December 13, 1904.⁴ He made a small incision above the umbilical level, to the left of the scar of the first operation. The liver was found to be partly, but not altogether, adherent, and as attempts to stitch the liver to the abdominal wall led to bleeding from the liver, he shut off the peritoneal cavity with tampons. He then bored a hole into the liver with a Paquelin's cautery about 3 centimeters deep, and on probing this a great deal of serous-looking fluid suddenly welled up from the opening, and the probe then passed down for 6½ centimeters from the surface, as if one of the large bile ducts, or a cyst

²Die Behandlung schweren Lebererkrankungen durch die Anlegung einer Leber-Gallengangsfistel, Berliner Klinik, October, 1902, Heft 172.

³H. Scheuer, Casuistisches zur Chirurgie der Gallenwege, Berliner klin. Woch., 1902, No. 7, p. 138.

⁴Calcium chlorid was, as usual, employed before this operation, and likewise before the previous operation, in order to lessen the tendency to hemorrhage.

filled with serous-like fluid, had been entered. A drainage tube was left in the opening.

Some of the fluid which escaped at the operation was examined, and found to contain very little albumin; in fact, not more than could be accounted for by admixture with blood. No hydatid hook-lets were seen.

The patient rapidly recovered from the effects of the anesthetic, and seemed quite comfortable. In the evening following the operation his temperature was 100° F. The next morning (December 15) it was 99° F., rising in the evening to 100.4° F., after which it remained below 100° F. The amount of fluid discharged from the liver was enormous, and on December 16 it was all allowed to run through a long drainage tube from the wound into a bottle beneath the bed, where it was collected and measured every day. On December 16 it was clear orange-brown in color, and not tinged with blood; the specific gravity was 1006; it was of neutral or slightly alkaline reaction, and yielded a very considerable "cloud" of nucleo-albumin on the addition of acetic acid in the cold. As the precipitate, after boiling and acidifying, was scarcely greater than after adding acetic acid in the cold, it was concluded that the fluid contained hardly any serum albumin. Though it yielded an intense Gmelin's reaction, no Pettenkofer's reaction for bile salts could at first be obtained. It still contained some red blood-cells.

The discharge of the bilious fluid continued, but the daily amount greatly diminished, and it became darker in color. On December 26, 1904, we noted that the fluid was clear, limpid, of dark color from the presence of bile pigments, of specific gravity 1010, and of neutral reaction. A drop or two of glacial acetic acid, added in the cold, produced a considerable precipitate of nucleo-albumin, which was redissolved in an excess of the acid. On boiling without the addition of acid only a very faint "cloud" appeared, but on adding acetic acid the same precipitate was produced as by the acetic acid in the cold: a very faint "cloud," however, remained after adding excess of acid to the boiling fluid, and this very faint "cloud" may have been due to a trace of serum-albumin in addition to the nucleo-albumin. Sediment obtained by the centrifuge showed a few red blood-corpuscles, but no cholesterin crystals. Some of the fluid, which had been allowed to become concentrated by slow evaporation, showed the presence of leaf-shaped crystals and of

"rosettes" and "horse-comb" clusters similar to clusters of uric acid crystals, sometimes observed in artificially concentrated urines. On some occasions octahedral crystals, like those of oxalate of lime, were noted, as well as cholesterin plates.

Some of the fluid from the liver, on December 22, 1904, was sent to the Clinical Research Association to be examined for bile acids. The report then was that a positive Pettenkofer's reaction was obtained, and that, after treatment by Dr. Tyson's method, the fluid also answered to Oliver's test (peptone solution), and to Pettenkofer's test, so that there could be no doubt that bile salts were present.

The specific gravity of the fluid varied slightly. On one occasion, as already mentioned, it was 1010, but on December 31 it was again only 1006. On January 5 the daily quantity of fluid from the biliary fistula was only 200 cubic centimeters, and as it escaped at the sides of the long drainage tube the latter was discontinued after that date, the fluid afterward being allowed to collect in the dressings, which had to be changed twice daily.

The following table shows the daily quantity of the fluid from the biliary fistula, as long as it was collected in a vessel; that is, until January 5. The daily amount of urine is likewise given.

Date.	Daily Amount of Fluid from Biliary Fistula.	Daily Amount of Urine.
December 17, 1904.....	2300 c.c.
December 18, 1904.....	2000 c.c.
December 19, 1904.....	2400 c.c.
December 20, 1904.....	2000 c.c.	1000 c.c.
December 21, 1904.....	1650 c.c.	1100 c.c.
December 22, 1904.....	700 c.c.	750 c.c.
December 23, 1904.....	2000 c.c.
December 24, 1904.....
December 25, 1904.....	400 c.c.	1700 c.c.
December 26, 1904.....	750 c.c.	700 c.c.
December 27, 1904.....	250 c.c.	750 c.c.
December 28, 1904.....	400 c.c.	1500 c.c.
December 29, 1904.....	1000 c.c.
December 30, 1904.....	300 c.c.	1100 c.c.
December 31, 1904.....	200 c.c.	1300 c.c.
January 1, 1905.....	250 c.c.	1250 c.c.
January 2, 1905.....	1750 c.c.
January 3, 1905.....	400 c.c.	1750 c.c.
January 4, 1905.....	1700 c.c.
January 5, 1905.....	200 c.c.	1400 c.c.

We must now describe the patient's condition after the operation, an operation which might be termed an "intrahepatic cholan-

giostomy," or "lepatostomy," that is, the artificial production of a hepatic fistula. Though he was free from fever, and quite cheerful, and took his food fairly well, and though the jaundice diminished, and the liver became smaller, he steadily became more emaciated. The feces, of course, remained perfectly colorless, but the urine became less bilious. Occasionally there were attacks of vomiting, and on one occasion the vomit apparently contained altered blood. At the commencement of January there was much purulent expectoration, and impairment of resonance, with crepitation, in the right infrascapular region.

In the middle of January, 1905, the diminution of the jaundice was very striking, and on February 2 the icteric tinge had practically disappeared from his skin and sclerotics. About this time the liver had decreased so much in size that the lower border, in the right nipple line, was about the level of the umbilicus: in fact, the lower border had risen as much as the attachment of the front of the liver to the abdominal wall in the neighborhood of the biliary fistula would allow. The urine on February 2, 1905, gave no distinct Gmelin's reaction, though it turned red on the addition of nitric acid. It was clear, of medium color, acid reaction, and free from albumin, and—what we believe to be a very noteworthy point—free from nucleo-albumin, the addition of acetic acid in the cold giving no precipitate or turbidity.

By the middle of January the patient had lost about 14 kilograms (31 pounds) in weight since the operation, but after that he began gradually to increase in weight, gaining 5 kilograms (11 pounds) by the end of the month.

Early in February he commenced to have irregular fever. On February 7 slight edema and purpura of the legs was noted after he had sat up in the ward. On February 13, there was much edema of the loins, and the patient was manifestly losing strength. The slight purpuric eruption on the legs was still present. There was impairment of resonance in the left infrascapular region. The urine was of specific gravity 1020, acid, clear, of medium color, giving no Gmelin's reaction, and free from albumin and excess of nucleo-albumin. Increased feebleness was followed by death on the morning of February 16.

The accompanying chart (Fig. 1) shows the temperature, pulse, and daily amount of urine during the last weeks of the patient's life.

The *necropsy*, performed by Dr. Weber, February 16, 1905, showed the body to be much emaciated, and the front of the chest somewhat sunken on the right side. Examination of the head and brain showed nothing special, excepting the "turritiform" shape of the skull, already alluded to, which was found to be associated with synostosis of the frontal and parietal bones, with complete obliteration of the sagittal and coronal sutures. The brain weighed 48 ounces (1450 grams). The heart was rather small, weighing only 8 ounces (240 grams). Otherwise it showed nothing peculiar. The right lung was completely and very firmly adherent to the chest wall, and was not removed for careful examination. The left pleura contained some serous effusion. There were some nodules, which to the naked eye appeared like metastatic tumors, in the left pleura, and in the left lung itself. At the apex of the left lung was a little old

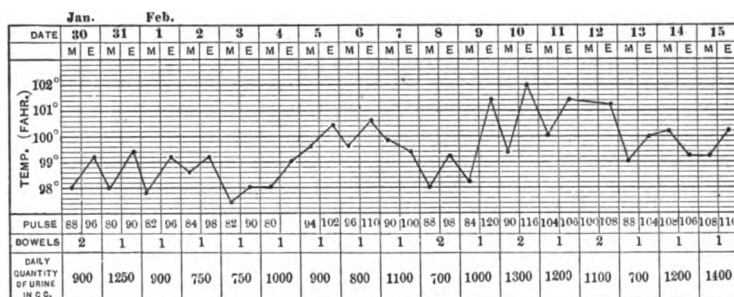


FIG. 1.—Chart showing temperature, pulse-rate, etc., during last weeks of the patient's life.

scarring, and some of the bronchial glands were enlarged, partly pigmented and partly caseated. The liver was firmly adherent to the abdominal wall in front. The fistulous opening on the front of the abdomen, for the production of which the second operation had been performed, was found to communicate by a very narrow channel with one of the intrahepatic bile ducts. Great contraction had evidently taken place since the time of the operation, but the track was still open. Evidently owing to this biliary fistula none of the bile ducts in the liver were dilated. The liver was apparently not enlarged, as when separated from the surrounding parts it weighed only about 50 ounces (1500 grams). Its substance was rather firm, and everywhere of a dark-green color. It contained no new growth of any kind or calculus. The gall-bladder was of moderate size, and filled with very sticky, inspissated blackish-green bile. The transverse fissure of the liver, including the whole region of the

junction of the cystic, common, and hepatic bile ducts, was occupied by a non-encapsuled, rather tough growth, resembling connective tissue. With probe and scissors it was possible to follow the channels of the various ducts most of the way through this growth. No calculus was found anywhere. The duodenal end of the common bile duct was pervious and apparently not in any way diseased. In the neighborhood of the hilum of the liver were some enlarged lymphatic glands. There was a good deal of serous peritoneal effusion. Scattered over the peritoneum were nodules, supposed at the time of the necropsy to be metastatic tumors. The omentum was collected into a tough mass, and seemed to the naked eye to be infiltrated with growth, and there was evidence of chronic peritonitis, with considerable thickening of the whole serous coat of the stomach,⁵ such as is not rarely met with in cases of diffuse peritoneal cancer (the so-called "cancerous peritonitis"), sometimes after operative attempts to remove a primary growth. The spleen weighed only 4 ounces (120 grams), and contained one nodule of apparent growth. The kidneys weighed together 11 ounces (330 grams), and one of them, it may be remarked, showed a peculiar congenital abnormality, the pelvis and the ureter being attached to the ventral surface instead of in the usual position. The pancreas appeared to be quite normal. Of the suprarenals one only was examined, and appeared normal. The peritoneal coat of the stomach was, as has already been mentioned, considerably thickened. The intestines showed nothing peculiar (excepting the growths on their peritoneal surfaces, already mentioned), neither did the testicles. The left humerus was sawn through longitudinally, so that the bone-marrow of the shaft might be examined. This was of red color throughout, and of gelatinous consistence.

Microscopical Examination.—Sections of 24 different pieces from various parts were prepared. The tough connective tissue-like mass from the hilum of the liver filling up the transverse fissure was found on microscopic examination to consist of adeno-carcinomatous tissue (malignant adenoma). The microscopic sections (two pieces of the growth were examined) showed tubules (Fig. 2) lined by columnar-celled epithelium, cut across in various directions. The

⁵ Superficially the stomach resembled an early stage of the so-called "leather-bottle stomach." *Vide* A. W. Nuthall and J. G. Emanuel, Diffuse Carcinomatosis of the Stomach and Intestines, *Lancet*, Jan. 17, 1903, p. 159.



FIG. 2.—The primary adenocarcinoma at the hilum of the liver, showing tubules of various sizes and shapes, one with its lumen filled with cells, or intracystic growth. $\times 110$.



FIG. 3.—Portion of the growth, showing penetration of carcinomatous tubules into a nerve. $\times 110$.



FIG. 4.—Section of the liver showing a certain amount of interacinous biliary cirrhosis. $\times 110$.

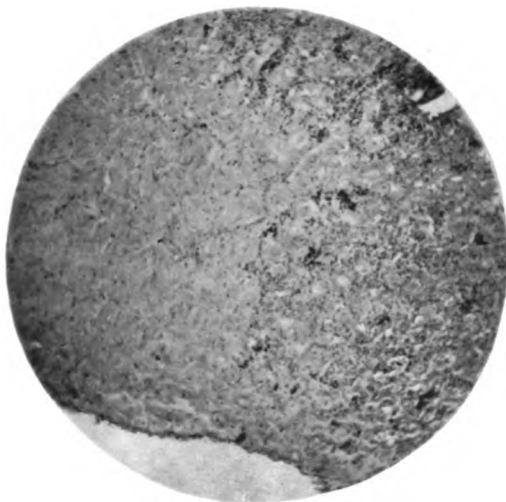


FIG. 5.—Section of the bone-marrow from the shaft of the left humerus, showing an erythroblastic reaction on one side and gelatinous degeneration on the other. $\times 120$.

tubules were of various sizes and shapes, some of them being large enough to appear in transverse section as cysts (lined by columnar epithelium). In some parts tubules were to be seen inside larger tubules (intracystic growth), and a few of the tubules were lined by less distinctly columnar (more spheroidal-like) epithelium, and were filled up with cells so as to show no lumen. The tubules were separated from each other by a variable amount of connective tissue; in some parts they were close together, as in adenomas, but in other parts they were widely separated by connective tissue. Though the tubules were mostly lined by only a single layer of cylindrical epithelium, and in their regularity reminded one of adenomatous growths,⁶ they were found to have invaded the structures at the hilum of the liver, penetrating between, and, in one or two places, into the nerves (Fig. 3). The growth was not encapsuled, and was evidently malignant, although, as we shall presently have to point out, no metastasis had as yet occurred, at least none that could be recognized. It was, therefore, a primary adeno-carcinoma or malignant adenoma, which, owing to its position, doubtless originated from the extrahepatic bile ducts at the hilum of the liver. We shall return to this subject later on.

Examination of the liver (Fig. 4) itself showed a certain amount of fibrosis between the acini, with increase (at least apparent increase) in the number of the biliary canaliculi: in fact, the appearances found in cases of biliary cirrhosis due, directly or indirectly, to obstruction in the large bile ducts.⁷ One or two circular spots of cellular infiltration suggested commencing tubercle formation, but a section was specially stained for tubercle bacilli, with a negative result.

The supposed metastatic growths from the lungs and spleen and from the peritoneal surfaces of the jejunum and ileum, as well as the thickened omentum, the thickened outer wall of the stomach and the lymphatic glands from near the hilum of the liver, were found by microscopic examination to show the typical changes of tuberculosis with giant-cell formation, more or less caseation, etc. Sec-

* The tubules of adenocarcinoma of the rectum may, of course, also be well-formed and lined by a single layer of epithelium.

⁷ F. Parkes Weber, *Biliary Cirrhosis of the Liver, with or without Cholelithiasis*, *INTERNATIONAL CLINICS*, 13th Series, 1903, vol. iii, p. 57; *Transactions of Pathological Society of London*, 1903, vol. liv, p. 103.

tions stained for tubercle bacilli showed their presence in the thickened wall of the stomach, in the omentum, and in nodules from the lung, spleen and jejunum.

Sections of the bone-marrow from the shaft of the left humerus showed typical "gelatinous degeneration." The degenerated tissue consisted of an almost homogeneous substance containing only a few erythroblasts and other cells, and the remains of fat vesicles. At one part of the field shown in Fig. 5 there is, however, a decided erythroblastic reaction. The tissue at this part is rich in cells, almost all of them being erythroblasts, with typical deeply-stained homogeneous-looking nuclei, some of them with two nuclei or a lobed nucleus, probably in process of division. Here and there large numbers of erythroblasts are grouped together in dense clumps.

The question of diagnosis claims our attention. At one time, especially after the negative result of the first operation (exploratory laparotomy), we almost regarded the case as one of Hanot's disease, that is to say, hypertrophic cirrhosis of the liver with chronic jaundice. The points against this diagnosis were: The absence of great enlargement of the spleen, the comparatively recent and sudden development of the jaundice, and of the hepatic affection altogether, and the complete absence of biliary pigments from the feces. It was this latter point which finally made us come to the conclusion that the cause of the jaundice and hepatic enlargement was some mechanical obstruction (probably not a calculus)^{*} at the hilum of the liver, and owing to the absence of distention of the common bile duct and gall-bladder Dr. Michels thought that this obstruction was situated proximal to the junction of the cystic and common ducts. We, therefore, concluded that the bile ought to be drained off externally, and Dr. Michels succeeded in effecting this by the establishment of a hepatic fistula in the way described. In fact, the jaundice practically completely disappeared, the urine became free from biliary pigments, and the liver shrank, so as to weigh about the normal amount at the time of death. It is probable that the spleen also became smaller with the relief of the jaundice,

* There was no history of biliary colic or of previous jaundice or of attacks of fever such as are frequently met with in cholelithiasis. Moreover, it must be remembered that gall-stones in the hepatic and common bile ducts nearly always allow some bile to pass now and then.

as though it had been apparently enlarged by physical examination in the earlier part of the illness, it was found to weigh rather less than normal at the necropsy.

There is not much to be said in regard to the tuberculosis which developed. Minute carcinomatous metastases on the peritoneum and pleura often have the appearance of tubercles when examined by the naked eye at the time of a necropsy, or during an operation, but in the present case it was the tuberculous growths which at the necropsy appeared to us to be carcinomatous metastases. A striking example of the macroscopic resemblance of tuberculous growths to carcinoma has recently been recorded in Germany by Dr. E. Ruge.⁹ His patient presented all the signs of carcinoma of the pylorus: the typical tumor was felt, and there was absence of hydrochloric acid and of lactic acid from the gastric contents. The diagnosis of cancer of the pylorus was confirmed by laparotomy, and even at the post-mortem examination the disease was supposed to be carcinoma of the pylorus, with numerous metastases. It was only the microscopic examination which showed that not only the supposed primary tumor, but all the metastases, were in reality of tuberculous inflammatory origin. Ruge compared the carcinoma-like tuberculous nodules to *Perlsucht* in cattle.

The explanation of the development of the tubercle in our case is not quite obvious. The presence of some partially caseous bronchial glands and remains of pulmonary (apical) tuberculosis show that the patient had previously had old quiescent tubercle in his body. The outbreak may, perhaps, be regarded as a reawakening of quiescent and latent tuberculosis, facilitated by the patient's cachexia and diminished power of resistance. Secondary infection from without appears extremely improbable, but it is just possible that at the first operation tuberculous glands in some part of the abdomen or thorax may have been damaged. On the other hand, no bad signs were noted until after the second operation, and at this operation it is exceedingly unlikely that anything of the kind can have taken place, as the organs were not moved about or pressed upon. The type of the tuberculosis was remarkable, as we have already noted, especially in respect to the tumor-like growths on the peritoneal surface of the intestines and the diffuse tuberculous thickening of the outer coat of the stomach.

* Beiträge zur Klinik der Tuberkulose, 1905, vol. iii.

Primary carcinoma of the bile ducts at the hilum of the liver, without metastases and without the liver itself being invaded by the new growth, is not a common cause of chronic jaundice. H. D. Rolleston¹⁰ recently has pointed out that some cases described as primary cancer of the liver might possibly in reality have been cases of single large adenoma of bile ducts. In our case, however, the growth was a typical cylindrical-celled adenocarcinoma or malignant adenoma,¹¹ infiltrating the tissues at the hilum of the liver, and even penetrating into nerves.

J. Orth¹² says that primary cancer of the bile ducts, which is generally a cylindrical-celled adenocarcinoma, is a rare disease. "Its most usual situation is at the junction of the hepatic ducts or at the orifice of the choledochus." In our present case there can be practically no doubt that the growth originated at the junction of the two hepatic ducts to form the common hepatic duct, and that at the time of the first operation (exploratory laparotomy, October 7, 1904) the cystic and common bile ducts were not yet involved. At that time, although the obstruction to the exit of bile from the liver was complete, Dr. Michels found no dilatation of the gall-bladder or of the common bile duct, and was able to express some of the bile from the gall-bladder into the common duct. Doubtless the cancer could not be felt at the operation because at that time it was extremely small and situated deep in the transverse fissure of the liver, though at the time of death (February 16, 1905) it had already involved the junction of the cystic and common bile ducts.

We have already alluded to the fact that the present case confirms the view that chronic obstruction of the larger bile ducts leads gradually to more or less interstitial hepatic fibrosis, in the same way that chronic obstruction of a ureter, with hydronephrosis, leads to chronic fibrosis of the affected kidney.¹³ We lay stress on this point,

¹⁰ *Diseases of the Liver*, Saunders & Co., Philadelphia and London, 1905, p. 455.

¹¹ Rolleston (loc. cit., p. 688) thinks that spheroidal-celled carcinoma of an extrahepatic bile duct may possibly be derived from mucous glands in its wall.

¹² *Lehrbuch der spec. path. Anatomie*, Berlin, 1887, vol. i, p. 988.

¹³ *Vide* E. P. Weber, *Trans. Path. Soc. London*, loc. cit. In regard to this subject, our colleague, Dr. Fürth, has kindly allowed us to allude to the following striking case which was under his care at the German Hospital. The patient, a married woman, aged 66 years, commenced to suffer from jaundice

as it has been disputed by many. Amongst other writers on the subject, Scagliori¹⁴ has quite recently drawn attention to biliary cirrhosis as a result of obstruction by columnar-celled carcinoma of the large bile ducts.

As far as it went, the operation of hepatostomy (biliary drainage by intrahepatic cholangiostomy) was successful. It was only intended to relieve the jaundice and the retention of bile in the liver. The jaundice practically disappeared; the liver, though it could not, owing to adhesions, return to its normal position, returned to its normal dimensions (as judged by its weight), and the urine became practically free from bile and nucleo-albumin.¹⁵ But the tuberculous complication prevented the result from being really satisfactory, and we must also admit the possibility of the hepatic fistula closing up spontaneously had the patient lived longer, for the fistulous channel at the time of death had become extremely narrow.

The surgical aspect of the case requires but little comment. Where the situation of the obstruction is proximal to the junction of the hepatic and cystic ducts it would, of course, be futile to attempt to drain the gall-bladder or to make a cholecystenterostomy. Drainage of the intrahepatic ducts means a permanent biliary fistula (at least as long as the fistulous channel can be kept open), except in those cases in which, from the nature of the obstruction, a reopening of the natural biliary channels may be expected, as in the case pub-

for the first time in March, 1904. Apparently no bile passed into the bowel, and jaundice, emaciation, and weakness became extreme. She was tapped four times for ascites. The liver, which was at first greatly enlarged, with a somewhat uneven edge, diminished so much in size that just before her death (October, 1904) the edge could only just be felt below the costal margin. At the necropsy the gall-bladder, full of calculi, was surrounded by malignant growth, but the point which specially concerns us is that all the bile ducts, intrahepatic as well as extrahepatic, were so dilated as to remind one of the appearance seen in a hydronephrotic kidney. Microscopically, the minute biliary ducts were seen to be full of inspissated bile (by naked eye examination the substance of the organ was of a deep-green color as usual), and there was a certain amount of biliary cirrhosis. Yet so much had the liver diminished in size before death that it weighed only about 40 ounces (1200 grams). The heart was also very small, weighing only 5 ounces (150 grams).

¹⁴ *Il Policlinico*, November, 1904.

¹⁵ As if the excess of nucleo-albumin, which constitutes a striking feature of some bilious urines, were, like the bile-pigment, absorbed from the biliary passages into the blood, and then (again like the bile-pigment) excreted with the urine.

lished by Rotter.¹⁶ With a view to avoid a biliary fistula Kehr excised a piece of the edge of the liver, 6 centimeters long and 3 centimeters broad, made a corresponding opening into a loop of small intestine and stitched the edges of the intestinal opening to the margin of the wound in the liver. Kehr terms the operation "hepato-cholangio-enterostomy."¹⁷ In his case the jaundice was soon relieved, the bile passing from the exposed intrahepatic ducts straight into the intestine, but the patient survived only four weeks. It seems a somewhat hazardous proceeding to bring the wound of the liver into contact with the contents of the bowel. The establishment of a biliary fistula is certainly the safer proceeding, and the operation should be performed on the left side of the liver, as the chance of reaching a large bile duct is supposed to be better on the left side than on the right. The operation can be done with a trocar (Hirschberg) or preferably (as in the present case) with the thermocautery.

We will only add a few words on the change in the bone-marrow. This consisted in a mixed erythroblastic reaction and "gelatinous degeneration," the latter predominating. It is well to ascertain as far as possible the bone-marrow changes associated with various clinical conditions. According to Roger¹⁸ and Muir,¹⁹ extreme inanition and emaciation seem to be the chief causes of gelatinous change in the bone-marrow, and great emaciation was certainly present in our case.

In conclusion, we have to thank the residents at the German Hospital, Dr. Schuh, Dr. Mülberger, Dr. Schenck, and Dr. Daser, for their many and excellent microscopic preparations from the case, and we are also greatly indebted to Dr. H. D. Rolleston and Mr. S. G. Shattock for their kindness in looking through the sections with us.

¹⁶ Loc. cit.

¹⁷ Centralblatt für Chirurgie, 1904, No. 7, p. 185. See also Enderlen and Zumstein, "Ein Beitrag zur Hepato-Cholangio-Enterostomie," Mitteilungen aus den Grenzgebieten der Med. und Chir., Jena, 1904, vol. xiv, p. 104.

¹⁸ Roger and Josué, Comptes rendus de la Soc. de Biologie, Paris, 1900, p. 417.

¹⁹ R. Muir, Trans. Pathological Soc., London, 1902, vol. liii, p. 392.

Surgery

FRACTURES OF THE PATELLA

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THE patella is a sesamoid bone developed in the tendon of the quadriceps extensor muscle. The tendon from the patella to the tubercle of the tibia is called the ligamentum patellæ. The rectus and crureus muscles are inserted into the upper border of the patella. The vasti are inserted into the lateral borders of this bone. The general fascia extends downward and is continuous with the capsule of the knee-joint. In front the patella is full of holes for the entrance of blood-vessels. On its surface are a number of longitudinal striæ. Quite frequently there is a considerable transverse furrow at or near the junction of the middle and the lower thirds. More of the patella rests and moves upon the external condyle or the femur than upon the internal condyle. The fibers of the internal vastus extend lower than those of the external vastus, and they pull more transversely on the patella: this appears to diminish the tendency of the patella to dislocation outward. This tendency can arise in part from the fact that the femur meets the tibia somewhat obliquely. The posterior surface of the patella is somewhat oval in shape, and has two parts, the greater of which is related to the external condyle, the lesser to the internal condyle. The patella always moves with the leg during its flexion and extension, since it is attached to the tibia by an inextensible ligament. This ligament has a variable length, so that the patella does not have the same relative height in different persons. In any position it is in contact with the femoral condyles, over which it moves.

The mechanical relations of the patella deserve the surgeon's careful consideration. The patella keeps the tendon of the quad-

riceps extensor spread out, so as to prevent it from being gathered up into a round cord which might be forced into the cancellous tissue of the femoral condyles. This bone varies much in size in different persons, being better adapted to perform its function in one than in another. The patella is only a part of the tendon of the quadriceps extensor, and may be broken without there being a complete rupture of the entire tendinous structure. The meaning of this fact will appear in due time. During extension there is a direct muscular pull on the patella. As the leg is flexed more and more, there is a greater transverse stress put on the patella by the action of the quadriceps extensor. The import and meaning of this fact is, that the great strain, if any, is applied to the anterior surface of the patella. The pull of the quadriceps is at times very great,—and it may easily reach 2000 pounds, as may be readily demonstrated.

To any one who has made an examination of normal patellæ, as well as those which have been broken, it will be plain that there is much variety in the size and structure of this bone. That a small and fragile patella is more likely to suffer fracture than a firm and large one needs no argument to prove. And, in addition to this, we have two facts of importance: The more porous and probably more fragile part of the patella is in front; and, in a state of more or less flexion of the leg, this part in front is subjected to greater stress from muscular pull. And then the active causes of fracture of the patella are external violence and contraction of the quadriceps extensor. These causes may act separately or at the same time.

Let us analyze the muscular cause of fracture of the patella, since it has been considered the most frequent: The pull and stress are applied directly or indirectly. It requires a greater direct than indirect pull to break the patella, for reasons that will soon be stated. A direct pull of the quadriceps extensor can only occur when the leg is extended. And the fracture is produced in the following manner: A man with a fragile patella and a strong quadriceps raises his foot and makes a kick; the leg when fully extended must suddenly cease to move, being held by the posterior ligament and the ham-string tendons; the quadriceps has contracted with great force; and this force meets with an insuperable obstacle; the contraction is arrested suddenly; the muscle ceases to shorten at once; the impact—or pull—of the entire force of the muscular contraction is applied to the patella; not only is there a pull of 1000 or

2000 pounds, but this pull is applied suddenly by the sudden arrest of the extension of the leg; the element of velocity, which augments the force of the pull, is introduced, and the knee-pan breaks.

When the leg is more or less flexed the pull of the quadriceps extensor on the patella is indirect, and then, from the nature of the mechanical relations, there is more or less cross-stress or cross-strain put on the patella. This must be so for the following reasons: The posterior surface of the patella rests on the femoral condyles; and as this surface is often somewhat oval, it may rest on the most prominent part; this would make it a lever of the first order, so that it would be subjected to frequent cross-stress. Let the leg be flexed: The pull of the quadriceps would be more applied to the anterior than the posterior part of the patella, while the posterior part would be subjected to greater compression. The *ligamentum patellæ*, the anterior part of the patella, and the *tendo patellæ*, represent a greater curve than the posterior part of the patella with its tendon and ligament: so that, in cases of sudden muscular contraction, the anterior part of the patella receives the pull that would be applied to the entire bone, if the leg were extended. And then the anterior and porous structure of the patella begins to separate first, whereupon the fracture extends backward through the entire bone.

Not only is there an upward pull on the patella, but there may be a lateral one as well. For instance, when the leg is flexed to a right angle to the thigh, the fibers of the vasti muscles must pull from side to side on the patella. The internal vastus pulls inward and upward to some extent. The external vastus pulls outward and upward to perhaps a less extent. Thus it can happen that the vasti muscles, acting on opposite sides, may apply a lateral stress and perhaps strain on the patella, and tend to cause a vertical fracture.

It is easier to understand the application of external violence as a cause of fracture of the patella, even if the bone is less frequently broken in this way than by muscular contraction. For the patella is in an exposed position, and can be reached by a moving body, or it can come in contact with one that is immovable. The patella, in any position, projects beyond the femoral condyles, so that it will come against a hard body sooner than the lower extremity of the femur. It must be kept in mind that the position of the patella is marked by the position of the leg, as it is more or less flexed. The patella is about two inches in length and is, therefore, large enough

to move against or be struck by a variety of hard bodies. If the blow is severe enough, if the fall is far enough, the knee-pan will be broken.

It is clear that external violence and muscular contraction can coöperate in the causation of fracture of the patella. One or the other of these causes may operate first, or they may operate at the same time. A blow or a fall might cause an incomplete fracture, and then the quadriceps extensor might pull the fragments apart altogether. The quadriceps extensor might cause a cross-strain of the patella, which would then be completely broken by a fall or blow.

Causes that are correlated to and coöperate with external violence and muscular contraction in producing fractures of the patella may be mentioned: These fractures are uncommon in early life. *Malgaigne* saw one in a boy 11 years of age. *Hamilton* had a case in a boy 5 years of age—a small piece being broken off by direct violence. They are more common in middle life. They may reach 2 per cent. of all fractures. They are not common in old age; but as there are fewer old than young people, they are relatively more common in advanced life. Fracture of the patella occurs more frequently during the cold part of the year, when wet and icy foot-ways make falls more numerous, and when attempts to prevent falling bring into active contraction the quadriceps extensor. A person's occupation may expose him to falls and blows on the patella, as well as to extreme contraction of the quadriceps extensor, so that he may be peculiarly liable to fracture of this bone. This may be one of the reasons why fractures of the patella are more frequent in males than in females. Yet it would seem as if aged women were more liable to have this fracture than aged men, perhaps because their patellæ are more apt to become fragile on account of osteoporosis. Finally, I have long been of the opinion that fractures of the patella are more common among inhabitants of cities than among those of the country, since these predisposing causes are more active.

The following cases illustrate the causation of fractures of the patella:

CASE I.—Mrs. N., 45 years of age, was going down some stone steps, when she felt and heard a crack in her right knee. Then she fell down three steps and struck the same knee against the edge of a coping-stone. She was carried into her house. She sustained a

transverse fracture of the right patella near the middle, and a complete rupture of the ligamentum patellæ just below the inferior fragment. The rupture of the ligament was caused by muscular action and the fracture was caused by the edge of the coping. The fragments were wired, with a good result.

CASE II.—Mrs. B., 36 years of age, and six months pregnant, was going down some steps in a dimly-lighted place when she quite suddenly brought her weight down on her right leg, and felt and heard a crack in her right knee. She fell and when raised to her feet could walk some if supported. She received a transverse fracture of the right patella near the middle. There was no operation, and the ligamentous union gave a fairly useful limb.

CASE III.—A boxmaker, 25 years of age, was running on the pavement, brought his weight forcibly on his left leg, and felt something snap and give way in his left knee. He fell to the ground and could not get up. On the day of the injury he was brought to the hospital with a transverse fracture of the patella near the middle. The prepatella fibrous tissue was sutured, with fair result.

CASE IV.—A seaman, 45 years of age, while walking fell and struck his right knee on the deck of the vessel. When he got up and walked about he suffered pain, and was brought to the hospital, where a transverse fracture just below the middle of the right patella was easily made out. The lateral fascia and the fibrous tissue were untorn and held by the fragments in close apposition. No operation was performed, and the union was firm and the motion good.

CASE V.—A sailor, about 50 years of age, slipped on the deck of his vessel and tried to save himself from falling, but he came down on his right knee. He got up and could walk some, yet it was with a limp. He was brought to the hospital for a bruised knee. A careful examination disclosed the fact that there was a fracture of the patella without displacement of the fragments: these were held in place by the lateral fasciæ and the untorn fibrous tissue in front of the patella. This fracture was nearly transverse and just above the middle of the bone. Union was firm without operation.

CASE VI.—A young man, 23 years of age, was sparring and sprang backward on his left leg, when he felt something give way in his knee. He fell to the ground and could not get up. I saw him soon afterward and found the left patella broken transversely just

below the middle. I operated, wiring the fragments. There was some limitation of motion.

CASE VII.—A sailor, 22 years of age, fell into the hold of a canal-boat, and came down on his feet and then on his right knee. He was carried on deck, where I saw him a few hours later, and found him suffering much pain, with a transverse fracture of the right patella just below the middle. This patient had a refracture some time afterward, and then I wired the fragments.

CASE VIII.—A laborer, about 55 years of age, was riding on the front step of an open horse-car, and a passing truck-horse kicked his left knee. The patella was broken into six or eight pieces. The soft parts were severely injured. There was a large wound, making the fracture compound.

CASE IX.—A plasterer, 50 years of age, became intoxicated, and, as he was trying to walk, fell down on his left knee, striking the patella on a cobble-stone, and breaking it into several pieces.

CASE X.—Mrs. —, about 35 years of age, as she was going to step on the sidewalk from the street tripped and fell, striking her left knee against the edge of the curbstone. She was carried a short distance into the house, where I saw her soon after the accident, and found a transverse fracture of the right patella near the middle.

CASE XI.—A laborer, 65 years of age, slipped on the street pavement, and as he fell his right knee came against the edge of the curbstone. He was picked up and carried home, where I saw him with his family physician, and found a piece of the apex of the patella broken off by the external violence. The fragment was less than half an inch in diameter. The fibrous tissue was sutured, with fair result.

CASE XII.—Dr. S——, about 45 years of age, was walking on a defective sidewalk, when he tripped and then tried to save himself from falling; he came down on both knees, and broke both patellæ at once. The direction of the fracture of the right patella was from without inward and downward. The direction of the fracture of the left patella was nearly transverse. No operation was performed, and he had permanent disability.

CASE XIII.—A saleswoman, 40 years of age, and very stout, twisted her right knee and felt it snap, and then she fell to the floor. She was unable to get up. When I saw her there was some contusion of the lower and front part of the knee. I could make out a trans-

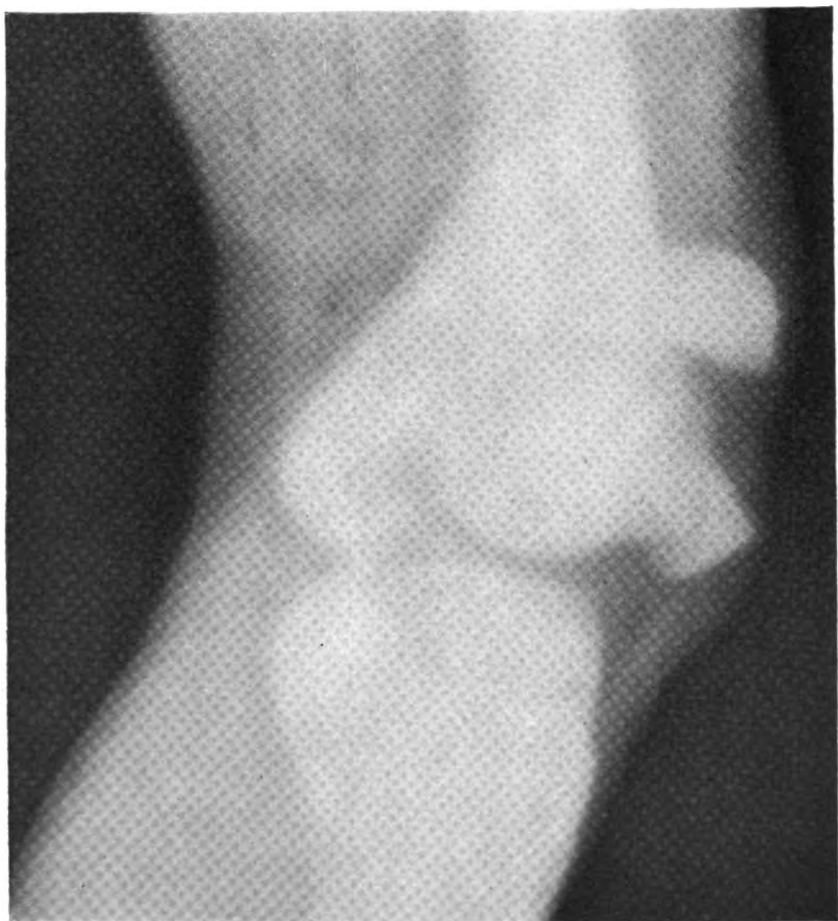


FIG. 1.—Radiogram of a fractured patella (left).

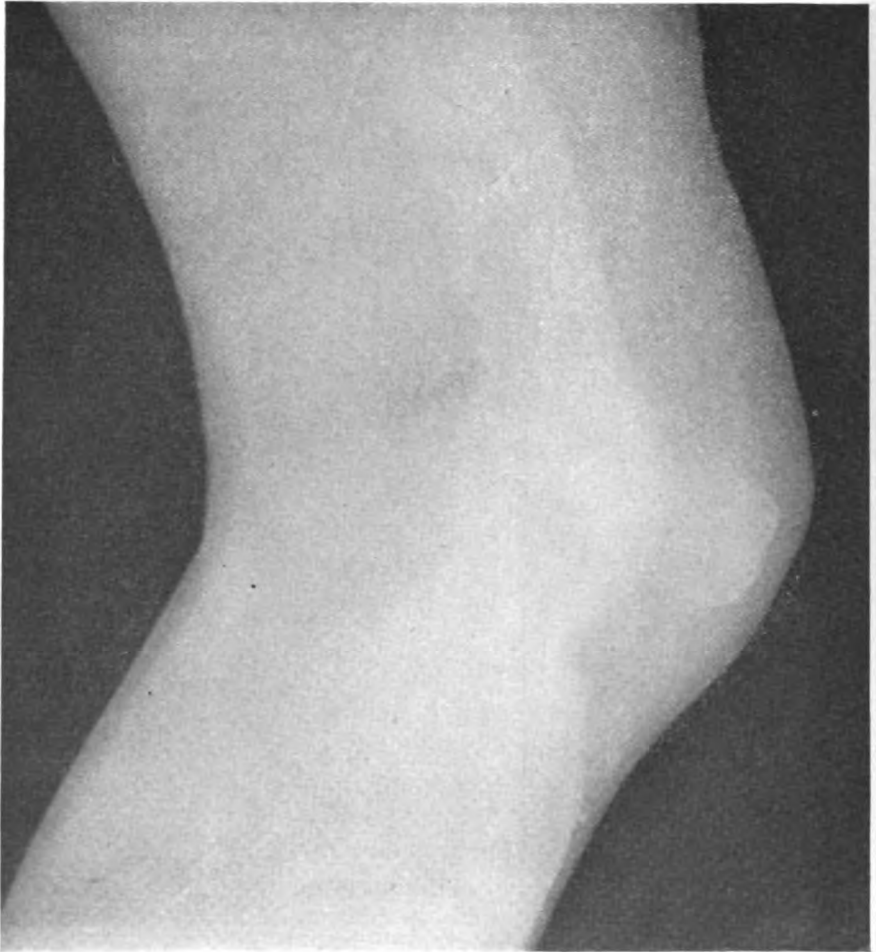


FIG. 2.—Radiogram of a fractured patella.



FIG. 3.—Radiogram of a fractured patella (right).



FIG. 4.—Radiogram of a fractured patella (right).

verse fracture of the right patella, as well as a rupture of the ligamentum patellæ near the apex of the lower fragment. She was treated by wiring and suture of the ligament.

CASE XIV.—A gentleman, about 50 years of age, came to my clinic for advice. He had broken his right patella some years before, and there had been only ligamentous union of the fragments. In an effort to keep from falling, he broke the left patella by a vigorous contraction of the quadriceps extensor, and fell to the ground.

Bichat speaks of two cases that we may note:

CASE XV.—A soldier kicked at his servant, and broke his patella.

CASE XVI.—A patient was cut for stone, and then had a convulsion, by which both patellæ were broken at once. The quadriceps extensor pulled on one end of the patella, and the flexors of the leg pulled on the other end of it, through the medium of the ligamentum patellæ. The pull on both ends of the little bone broke it in two over the femoral condyles.

Two cases mentioned by Malgaigne are of interest:

CASE XVII.—A dancer heard a sudden crack in his limb while executing some movement, but he made several steps, when his knee bent up and he fell backward.

CASE XVIII.—A physician struck his knee violently against the wheel of a cabriolet, causing severe pain. As he was going down a staircase the next day, he slipped and held himself up by the baluster, when he felt a crack in the same knee, making a complete fracture of the patella.

Two cases are reported by Hamilton.

CASE XIX.—A lad, 5 years of age, received a direct blow on the knee, and had a small piece of the margin of the patella broken off.

CASE XX.—A woman, 80 years of age, fell fifteen feet and had a fracture of the patella, which was probably caused by a direct blow.

The seat, direction, and extent of a fracture of the patella are important. The fracture may be located in any part of the bone. It is most frequently at or near the middle. It is quite often just below the middle, in the vicinity of the transverse furrow that exists from time to time on the front of the patella. The apex of the patella may be the seat of the fracture. The separation may be

somewhere in the upper half of the bone. And the lateral margin may be broken off. The direction of the fracture is doubtless for the most part transverse, or nearly so. Yet, when the fracture has been quite transverse from side to side, I have known a backward obliquity to exist downward or upward in cases upon which I have operated. A fracture may be partly transverse and partly oblique, or it may be altogether oblique. Closely related to oblique fractures of the patella are those which are vertical. In both vertical and oblique fractures the fragments may be of equal or unequal size. These fractures are probably caused by direct violence. The separation in comminuted fractures of the patella may extend in various directions. The extent of a fracture of the patella comprises three questions: Is the fracture incomplete? Is the fracture simply complete? Does the fracture involve the soft parts in the vicinity of the bone? It is reasonably certain that incomplete fractures of the patella occur, such as we find in other bones. It would, perhaps, be impossible to detect an incomplete fracture of the patella, for mobility and crepitus would be absent. And the most we could be sure of would be that there was a contusion. Incomplete compound fractures have been observed.

CASE XXI.—I once saw such a fracture made by an adze, with which a young man cut into the lower part of his left patella.

CASE XXII.—A case is mentioned by Poland. A man fell and struck his knee against the edge of a cutlass, receiving an incised fracture of the patella.

CASE XXIII.—I saw the case of an intoxicated man, who fell and struck his right knee against a spike; he had a punctured fracture of the patella, from which there radiated several fissures.

It is reasonable to call these cases of incomplete fracture, for the bone is broken. It is of interest here to say that surgeons have divided the bony structure of the patella with a chisel, leaving the cartilage unbroken.

A fracture of the patella can occur, having only the bone broken and leaving the fibrous tissue in front of it unbroken. The layer of fibrous tissue on the anterior surface of the patella is generally torn asunder when that bone is broken. The fracturing force may not go beyond this tissue and the patella, leaving all other structures uninjured.

CASE XXIV.—A young sailor fell from the rigging to the deck

of his ship, and was severely injured; one of his injuries was a fracture of the right patella, the bone and the fibrous tissue in front of it being broken, while the adjacent soft parts were sound.

Generally, however, either at the time the accident happens, or subsequently, the adjacent soft parts are more or less torn. And perhaps these cases constitute the greater number. For the most part this additional injury is due to the action of the quadriceps extensor. This muscle continues its action beyond mere fracture of the patella, or, having lost the resistance offered by the unbroken bone, it applies its whole force on the lateral fascia and ruptures it on both sides. And then the lateral fascia may be more or less torn through, so that the upper fragment is displaced upward to a considerable distance, and so that the lower fragment moves away from it to a marked extent when the leg is flexed. In cases of compound fracture, as well as those caused by great external violence, the soft parts are often so severely injured that serious results may follow. The contusions and wounds are for the most part adjacent to the patella. And we have then to consider the severity as well as the extent of the injury to the soft parts that are in the vicinity of a fractured patella.

The following case bears on the questions above considered:

CASE XXV. — A seaman, about 18 years of age, fell 12 meters into the hold of a ship, and received a fracture of the right patella and a compound, comminuted, depressed fracture of the skull. He was brought to the hospital, where he died on the following day. The autopsy disclosed the following facts in regard to the injured knee: An incision about 25 centimeters in length was made in the median line over the patella, extending above and below. Under the tegumentary tissues was found an extensive extravasation of blood, occupying the space in front of the ham-string tendons, and going upward from the insertion of the ligamentum patellæ for about 20 centimeters. From this space were two openings through the prepatellar fascia, large enough to admit the finger into the knee-joint: the prepatellar bursa and the knee-joint were one continuous cavity, the fibrous layer in front of the patella having been completely ruptured. The finger could easily reach the femoral condyles and the anterior edge of the upper end of the tibia. The patella had been broken into three fragments of nearly equal size, one above and two below, the fracture between the lower frag-

ments being vertical. The upper fragment was fissured on its posterior surface somewhat transversely in three places: these tissues are strongly suggestive of the possibility of incomplete fracture of the patella. On the broken surface of the three fragments the blood had oozed out, and coagulated into a firm clot of about 1 centimeter in thickness and adhering so as to prevent their reduction. There was no blood between the ends of the femur and tibia. And the contiguous structures of these bones were uninjured.

CASE XXVI.—Depuytren saw a vertical fracture caused by a carriage-wheel passing over the knee.

CASE XXVII.—Cousté saw a vertical fracture in an artilleryman, whose patella was struck by a splinter from a gun-carriage.

CASE XXVIII.—Sir Astley Cooper states that a vertical fracture of each patella was found in a male body that was dissected in St. Thomas's Hospital in 1822.

If we take into consideration the fact that vertical fractures are caused by external violence, it is evident that we must conclude that there will be an involvement of the soft parts to a very considerable extent. And we may add that the injury may be severe as well as extensive. Malgaigne, from whose work the above cases are derived, says that Dupuytren and Sir Astley Cooper are the only surgeons who had given special attention to vertical fractures of the patella.

SIGNS AND SYMPTOMS OF FRACTURES OF THE PATELLA

The signs and symptoms of fractures of the patella are interesting and important. Quite often a sudden crack or snap is felt or heard in the knee, and the patient falls and cannot get up. Or the patient falls and strikes his knee against a hard body, and then lies prostrate and helpless. If you ask him to raise his leg, he makes the effort and fails. Lift him up on his feet, and generally he is unable to walk even on a level. Rare exceptions may occur, such as I have already noted. In most cases there is a transverse depression in front of the knee, into which the surgeon can put his fingers, and which becomes larger on flexing the leg. Exceptions occur to this rule, in which the fragments are held together by untorn tissues. The fragments can be moved by the surgeon's fingers, not only from side to side, but upward and downward. The lower fragment cannot be moved upward until it has been moved downward. In a case of vertical fractures of the patella, the fragments will have lateral

mobility. In a case of comminuted fracture of this bone, the fragments will move in various directions. As to crepitus: Sometimes it is readily found; and sometimes it is difficult or impossible to detect it, for the following reasons: The blood which oozes out on the rough, broken surfaces of the fragments coagulates in a short time into a firm adhesive clot, which prevents the surgeon from bringing them together, so as to rub one against the other. I have often seen firm adhesive clots on the broken surface of cancellous bone in various parts of the body. And in a number of instances I have verified their existence at autopsy, in cases of death taking place soon after grave accidents. These clots will be referred to under the head of treatment of fracture of the patella.

In regard to the displacements of the patellar fragments, I may make the following statements: The longitudinal displacement is the most remarkable, and it takes place by separation, which may be more or less extensive. In some cases there is little or no separation of the fragments. In a few cases I have seen the fragments separated as much as two inches, when the leg has been completely extended: recent cases are now under consideration. Every degree of separation between these two extremes may occur. In the greater number of cases the fragments have been separated about one inch. But the distance between the fragments is made greater as the leg is flexed more and more. As to the angular displacements: The broken ends of the fragments may tilt forward. And when the fragments are pushed together the torn ends of the fibrous tissue in front of the patella may be caught so as to prevent complete reduction. The fragments in case of vertical fracture are displaced laterally. The cause of this is the fracturing force, as well as the pull of the vasti muscles. For anatomic and mechanical reasons the internal vastus has a greater displacing power than the external. The greater part of the separation is caused by the pull of the vastus internus. The vastus externus has most of its lateral pull on the upper part of the patella. And we may state here that the lower fragment in a transverse of the patella may have an inward lateral displacement, on account of the pull of the inferior fibers of the vastus internus.

The impairment of power and voluntary motion gives us one of the striking features of this injury. The inability to walk is a frequent result; and it is very rare that a patient who has a broken

knee-pan can raise his leg as he lies on his back. When the bone only is broken the patient may have the ability to raise the leg by means of the quadriceps extensor: in two cases which I have reported the ability to do this was not entirely lost. It is more difficult to raise the leg than it is to walk, after fracture of the patella, for reasons that are readily seen. And we may remark that the impairment of the voluntary motion comes in part from the following facts: The development of the full power of a voluntary muscle requires the existence of an obstacle to be overcome and moved; take away the resistance of such an obstacle, and the power of a muscle is diminished; these conditions occur in the case of a fractured patella. And the impairment is not all in the fact that the leg is disabled for walking and cannot be raised, but it is also in the fact that the volition cannot accomplish a great amount of work in trying simply to shorten the muscles.

In other words, there is a circle of dynamic relations in the co-ordinate structures of the knee-joint: The nerves, the muscles, and the bony levers are dynamically related, that is, they are interdependent. Disturb one, and the others are put in disorder. When the patella is broken, the stimulus of resistance to the action of the quadriceps is impaired or lost. The circle of dynamic relations is injured, and inability is the immediate result. And this inability, which follows a fracture of the patella, and which it is so difficult to describe, is in many ways characteristic, and it must be seen and studied in actual cases before it can be understood and appreciated. And to the experienced surgeon it is very suggestive of the serious and grave injury that caused it. The patient has a sense of this inability, and at times feels greatly disturbed and suffers much distress.

In addition to distress and anxiety, the patient has the usual pain of injury, which is often very severe. And the pain is frequently augmented by the swelling that takes place soon after the fracture occurs. The swelling contains effused blood, which is abundant in the subtendinous synovial sac, in the prepatellar bursa, and sometimes in the torn and bruised soft parts. And at the same time there is an increase in the quantity of the synovial fluid. And so it happens that there is more or less extensive fluctuation in the tumefaction in front of the knee. Finally, there is discoloration of

the skin accompanying the deformity and the disability which follow a fracture of the patella.

In the great majority of cases there is no difficulty in making a diagnosis of a fracture of the patella. The signs and symptoms are clear and unmistakable, and constitute conclusive evidence of the existence of a fracture. But the conditions and circumstances which stand in the way of making a diagnosis deserve to be carefully considered.

CASE XXIX.—A female, 40 years of age, came under my care for an injury to the right knee. A diagnosis of fracture of the patella was made, because she felt a crack in the knee at the time of the accident, and because of her inability to walk or raise her leg, for there was so much adipose tissue around the joint that the fragments could not be detected by the hands.

CASE XXX.—A laborer, 46 years of age, fell on his right knee and caused very great swelling of the soft parts. The diagnosis of fracture of the patella was verified only after careful aspiration, when the fragments could be felt.

CASE XXXI.—A colored woman fell from a horse-car and injured her left knee. She had no treatment. Some time afterward she brought a suit against the railroad company to recover damages for fracture of the patella. The medical witnesses of both sides said there had been a fracture, followed by bony union. The plaintiff said the fracture occurred at the time of the accident. The defendant said it occurred at a previous time. The evidence to prove that there had been a fracture was a transverse furrow in the front of the patella just below the middle. An examination of the right patella disclosed the existence of a similar transverse furrow,—only it was larger than the other. And yet there was no claim that it had ever suffered a fracture. It has already been pointed out that the patella may have a transverse furrow that is normal,—and that may appear to be a depression where the fragments have had bony union.

Neither this normal depression, nor one made by the subcutaneous rupture of the prepatellar fibrous tissue, nor a depressed fracture of the front of the patella, ought to be mistaken as a sign of the separation of the fragments in a case of complete fracture. In order to aid in removing our doubts on this point, we may examine the uninjured patella, so as to have a standard of comparison for the one that is

supposed to have a fracture: in this way we may guide our judgment and prevent mistakes. And then we may take a needle and explore the depression or the furrow in the patella. If the point of the needle can penetrate deeply, we may suspect that there is a fracture. On the assumption of the existence of an incomplete fracture of the patella, we are not warranted in making severe flexion of the leg in order that we may obtain separation and mobility of the fragments. For it is evident that the fracture might be made complete, when the result would be much less favorable. In some cases, it is plain that we cannot make a diagnosis of fracture of the patella, even when such an injury exists, since the signs are not to be found: for then there is some obscure incomplete fracture.

From the time when the patient falls, when he hears a crack in his knee, feels great pain and walks a few steps, sometimes forward, yet mostly backward; when he gets up with the assistance of some one; when he lies helpless; when he has to be carried and put in bed; when he moans on account of his distress and suffering; when the disability from pain almost equals the inability from loss of power; when he lies for the most part on his back; when he lets his leg rest in an extended position, or permits it to be flexed,—till the surgeon sees him some hours after, the internal hemorrhage may be going on, causing swelling of the knee, and separating the bony fragments of the patella, so that we may have in operation the concurrent causes of muscular contraction and distention from extravasated blood. Then we may say that the size of the swelling, as well as the extent of the fluctuation, denotes the degree of separation of the fragments, and so to anticipate the progress of the case. As the blood is absorbed, as the swelling becomes less and less, and as the pressure of the distention is removed, the bony fragments may be somewhat approximated, and this time will be longer or shorter, say, from one to three weeks.

Malgaigne saw the separation of the fragments of the patella diminish in nearly the same degree as the fluctuation in two patients, a man and a woman.

CASE XXXII.—“In the former the fracture was direct; the separation on the eighth day was 14 millimeters; on the fifteenth it was reduced to 10 millimeters, and fluctuation had entirely disappeared between the fragments, although still perceptible above and at each side of them.”

CASE XXXIII.—“In the woman the bone had yielded to muscular contraction; on the ninth day the separation amounted to 35 millimeters; on the fifteenth day it was diminished to 25, and the fluctuation was almost gone; on the eighteenth there was only a separation of 2 centimeters, and no trace of the fluctuation.”

TREATMENT OF FRACTURES OF THE PATELLA

Before treating of the repair of fractures of the patella, and of the nature of the bond of union between the fragments, the following proposition may be stated: When the cut or broken surfaces of cancellous bone are brought closely together and held in contact for a sufficient length of time they will unite by bone.

The truth of this proposition is attested and proved by the following evidences: When one part of cancellous bone is driven into another part, making an impacted fracture, the fresh surfaces, being in apposition, will form bony union. A large number of specimens and cases of fracture have come under my observation, illustrating this result. It has often happened in my practice that the reduction of fragments of cancellous bone has been perfect enough to make them unite by bone. Indeed, it may be said in this place that the only cases of bony union of patellar fragments, which have occurred in my practice, have followed when I have cut down and freshened the broken bone, bringing the cut surfaces as closely together as possible and retaining them by wiring the fragments or suturing the fibrous tissue in front of the bone.

If bony union is quite often possible under the conditions above named, we ought to obtain it for the most part when these conditions are fulfilled. But the fact is that the bony union of the fragments of the patella is very largely exceptional, under the plans of treatment that have been carried out hitherto. I have seen patients that have been claimed to have bony union: the fragments have been close together and immobile, but show translucency to the x-rays. I have followed such patients for some months, and have invariably seen the bond of union elongate, so that there would be mobility in continuity of the patella. From Stimson's work on fractures I take two cases for illustration:

CASE XXXIV.—Dr. Edward T. Caswell quotes a case: All the force that could be used did not make the slightest motion between the fragments of the specimen, so very firm and close was the bond

of union; but three longitudinal sections made through the removed bone showed no points of bony union between the fragments.

CASE XXXV.—In a case reported by Berger the patella 10 years after the accident seemed identical with its fellow. Only when the leg was extended and the thigh was flexed could slight mobility be detected between the fragments. We may remark: In the report it is stated that "a slight transverse groove marked the seat of the former fracture." And yet the bone seemed identical with its fellow, which must, therefore, have been marked by a transverse groove. So that the transverse groove does not prove the existence of a fracture. Nor can we always be sure that the bond of union is made of bone.

If we ask the reasons for this absence of bony union, several present themselves: separation of the fragments; formation of blood-clots; interference of the torn ends of the prepatellar fibrous tissue; the normal tendency of cancellous bone-fragments to unite by connective tissue. To the presence of the extravasated blood and the pull of contracting muscles we may add the shortening of the ligamentum patellæ, as well as that of the tendo-patellæ, when we are accounting for the separation of patellar fragments. That this shortening takes place, and at the same time goes on slowly, actual measurements and physiology prove. In many cases the extravasated blood is slowly absorbed, taking some days before retentive apparatus can be applied to the fragments so as to keep them reduced. In fact, the soft parts may be so severely bruised that they will not bear the pressure of reduction appliances. In the meantime, the shortening of the tissues above and below the fracture will go on to that extent that complete reduction of the fragments will be very difficult, and perhaps impossible. And then there will be more or less interspace left between the broken surfaces; and this interspace interferes with bony union. Even if these obstacles are entirely removed, we have clots and tissues in the way of repair by bone.

In the autopsy above reported the blood-clots, found on the broken surfaces, were firm enough to prevent the complete reduction and apposition of the fragments until they were rubbed off by taking considerable time and strength. Evidently the clots would have been in the way of reduction, and would have been obstacles to bony union if the patient had lived. In cases upon which I have performed the operation of suturing the patellar fragments, I have seen a firm clot

or a dense fibrous incrustation on the broken surfaces. In the more recent cases the fibrous incrustation exists. Both the clot and the incrustation will interfere with reduction and prevent union by bone. It may be briefly stated that the clot does not organize, nor does the organization that takes its place form bone.

And it may be added that the organic fibrous structure, which is the outgrowth of the connective tissue of the bone, while it fails to become ossified, frequently does not form a bond of union between the fragments between which we may find a kind of new joint. Also the torn ends of the prepatellar fibrous tissue not infrequently get between the broken surfaces so as to prevent complete apposition of the fragments and interfere with union by bone. This obstacle exists from time to time, but I am inclined to think that it has been overestimated as an interfering cause. Our experience with such tissue is that it is apt to contract when torn off and left to itself. All my observations of knee-joints that have been opened after fractures of the patella tend to agree with this statement. Yet if the fibrous tissue is torn through above or below the seat of fracture, the longer end will certainly curl over the broken end of the fragment to which it is attached.

Other circumstances take place which are worthy of attention. Every surgeon who has examined the normal patella knows that it projects backward beyond the tendon and the ligament, and that it can be tilted or rocked like a lever on its fulcrum by pressing first against one and then the other side, when the quadriceps is relaxed; and he further knows such is the form and location of the patella that pressure on the tendon will tilt or raise the lower end of the upper fragment forward, and that pressure on the ligament will tilt or raise the upper end of the lower fragment forward also. The effect of this will be, that the two fragments will be brought together posteriorly, and that they will be separated anteriorly, so that they have an interspace, into which the bandage may compress the soft parts that are in front. This tilting of the fragments is apt to occur and be augmented by those appliances that are commonly used by surgeons in treating fractures of the patella. These same appliances heap up the soft parts in front of the seat of fracture, so that they are ready to be pressed between the ends of the bony fragments.

Finally, we know from observation that the union of fragments of cancellous bone is more apt to be fibrous than that of compact

bone; and the fragments of the patella are no exception to this rule. Then it seems to be true that fragments which overlap are more frequently united by bone than those which are separated. So that we have two unfavorable conditions for bony union: Cancellous structure and separation of the fragments. When these things are so, we come to ask, What is the nature of the union that actually takes place? Let us illustrate this part of our subject:

CASE XXXVI.—A woman, about 45 years of age, brought a suit for damages against a manufacturing company, in whose employment she had broken her right patella the year previously. I examined her as a witness for the defendant, and found the fragments separated nearly three inches, and entirely without any intermediate bond of union. The broken ends of the fragments were smooth and rounded as could be felt subcutaneously.

CASE XXXVII.—A man, about 40 years of age, fell and broke his right knee-pan, and some time after he broke his leg. Some four years after the second accident there was a fibrous band two inches in length between the fragments of the right side; it was slender and not very strong: on the left side the fragments had no intermediate bond of union, and they had separated nearly four inches (Fig. 5).

CASE XXXVIII.—A gentleman, 84 years of age, had his left patella broken transversely when he was 20 years of age, and the fragments remained ununited, separated nearly three inches. He walked with a cane, and had been going upstairs backward for over 60 years.

CASE XXXIX.—A lady, 40 years of age, after refracture and long treatment of the left patella, had no union of the fragments, which were separated about two inches, the ends being covered by a firm fibrous incrustation. Another case in a sailor, previously mentioned, who was operated on, did not show any union of the fragments, which were separated two inches, and the incrustation was such as to prevent the process of repair and union.

CASE XL.—The following case of refracture is of interest: The primary accident has been mentioned previously. The transverse fracture of the patella had strong fibrous union less than one-half inch in length, and the ligament was slightly longer than before its rupture. This patient fell two years after the injury and broke the same patella as before, transversely through the other fragment, and then had firm fibrous union not more than one-third of an inch in

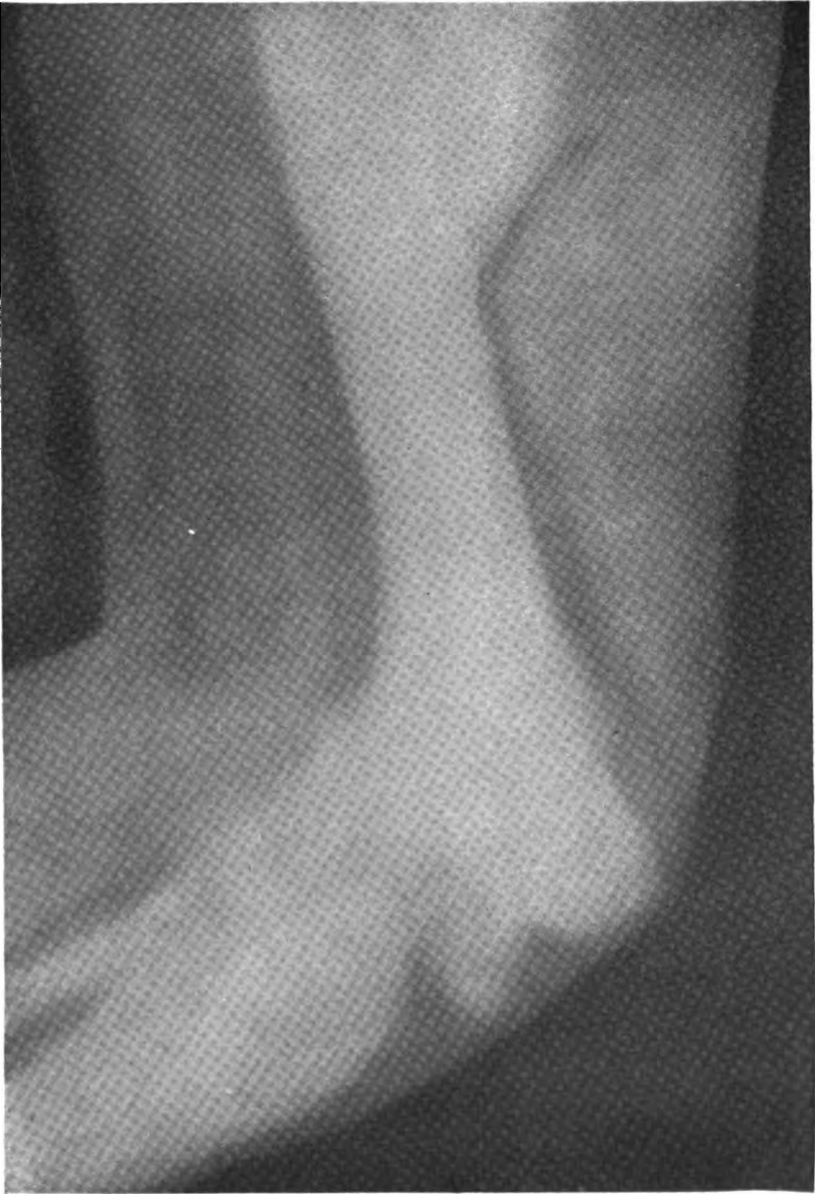


FIG. 5.—Radiogram of an old fracture of the patella.

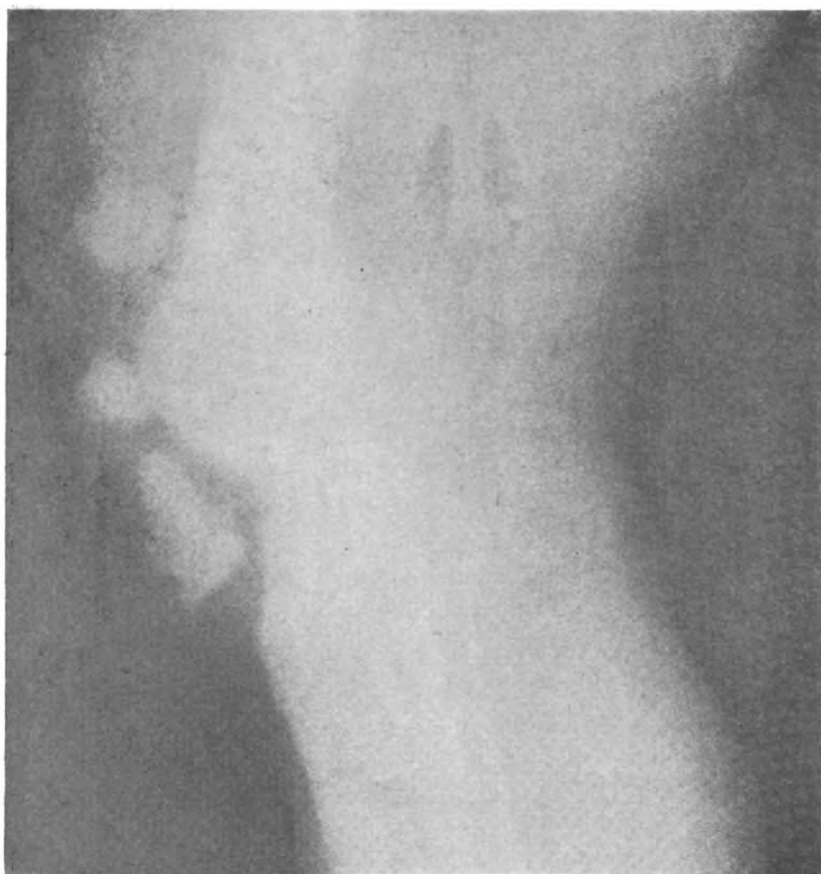


FIG. 6.—Radiogram of a fracture of the patella showing three fragments.

length. Slight depression could be felt at the seat of both fractures (Fig. 6).

CASE XLI.—Hamilton saw a man, 38 years of age, who, about three and one-half years before, had a fracture of the left patella, which had been treated with a plaster-of-Paris splint. The fragments were separated nearly four inches, and did not appear to have any bond of union. He had lost the power of voluntary extension of the left leg.

CASE XLII.—Also, a British soldier, 24 years of age, when he had a fracture of the right patella caused by severe external violence, 29 years after the accident had a straight limb, the fragments being separated two and one-half inches. No trace of a ligament or other bond of union could be felt.

CASE XLIII.—Also, a man, 56 years of age, fell upon his left knee and broke the patella transversely below the middle. Seventeen years after the accident Dr. Hamilton found the fragments separated three and one-half inches when the leg was extended. He found no bond of union between the fragments of any kind. Along the margins of the fragments the tendinous fibers of the quadriceps were prominent, especially on the outer side.

From Malgaigne's work I select the following cases:

CASE XLIV.—A patient, after fracture of the patella, had the fragments unite by a fibrous band that was very dense near its middle: during extension of the leg the separation between the fragments was 8 millimeters, and during flexion it was increased to 22 millimeters.

CASE XLV.—A man had a very thin fibrous band between the patellar fragments, which were separated an inch with the leg extended, and nearly an inch by flexion of the knee. The upper fragment was movable under the fingers, but it did not move with the flexion and extension of the knee, as if it had no extension with the other.

CASE XLVI.—The case of a member of our profession is cited as one of complete recovery, but the space between the fragments is about two-thirds of an inch: they are united by fibrous tissue.

In Holmes's System of Surgery there is a brief description of a specimen exhibited at the Pathological Society of London: The patellar fragments were united by a band of ligamentous tissue two and one-half inches in length. Also, there is a statement in regard

to another specimen, in which the bond of union is an aponeurotic structure, of considerable length, attached to the front of the upper fragment and to the broken surface of the lower one. Of thirty-one specimens examined by Mr. William Adams fifteen were examples of ununited fracture, twelve of true ligamentous union, and four were doubtful. In these ununited fractures the fragments may be separated to the extent of five inches, whereas in true ligamentous union the separation rarely exceeds one inch and a half. We learn from Bryant's *Surgery* of a preparation in the Guy's Museum showing the ligamentous union of four fragments, the lines of fracture being transverse, perhaps from different injuries. The united patella is much elongated.

The indications for treating fractures of the patella are to remove the displacements of the fragments. The most important displacement is one of separation. In the long bones the fragments overlap from muscular contraction; in the patella the fragments separate from the same cause. In speaking of the obstacles to bony union of the patellar fragments, we enumerated the obstacles to their reduction. These are: Swelling of the soft parts in front of the knee; extravasated blood in the anterior part of the joint; fibrous clots on the broken ends of the fragments; contraction of the quadriceps extensor. In one case, for instance, when the violence has not been great,—only sufficient to break the patella,—when the soft parts are slightly swollen, and when the lateral fascia is untorn, the hands of the surgeon can be so applied to the fragments as to reduce them. It is fortunate that quite a number of cases are of this kind. In fact, as we have already seen, there are a few cases, in which for reasons that have been given, the patellar fragments do not become separated at the time of the accident, and so only need retentive apparatus. In another case, when the fracturing force has been great, when the soft parts are much swollen, and when the fragments have been considerably separated, we cannot get at them for reduction. Then the primary indications are as follows: The extravasated blood must be removed as soon as possible, for it is in the way of reduction of the fragments: sometimes this may be accomplished by rest and bandaging; sometimes by the application of evaporating lotions; but not infrequently aspiration will be required. When absorption does not readily take place I am convinced that aspiration is safe. Then the fragments may be reduced, and a permanent retentive apparatus

applied. Yet in some cases more or less inflammation will occur: it will be necessary to subdue this before the reduction and the permanent retention of the fragments. In the meantime, the upper fragment will be drawn away from the lower; the quadriceps extensor will be somewhat contracted; the ligamentum patellæ will be shortened; the connective tissue will be changed in its relations; and some adhesions will be formed. According to the degree of the disturbance and the length of the intervening time, it will be more difficult to reduce the fragments, and will require more skill to keep them in place. And then another obstacle will remain: the fibrous clots on the ends of the fragments. In practice, I have seized them firmly between my thumb and fingers, and rubbed the clots off as well as I could, by means of a to-and-fro motion. I have thought that I obtained in this way a better reduction of the fragments, which united by a more desirable fibrous band.

As to the position of the body, the thigh, and the leg, during the treatment of fracture of the patella, we may say: The greater part of the quadriceps extensor has its origin on the thigh-bone, and, so far, the position of the thigh or the body cannot materially affect the displacement of the upper fragment. Only the rectus femoris spans the hip-joint, and even this part of the quadriceps has its two points of origin so near the head of the femur that the flexion of the thigh cannot greatly diminish the muscular pull on the upper fragment. It may be that a pull on the rectus, however slight, may cause a co-ordinate contraction of the crureus and the vasti,—as it were, by an irradiate irritation. At any rate, surgeons have generally elevated the thigh and raised the body, to a greater or less extent, in the treatment of fractures of the patella: and this is now a well-established practice. As to the position of the leg, there is only one opinion that is safe, and only one practice that is sound: The leg should be extended, for flexion of the knee moves the lower fragment away from the upper, while extension reduces it. Only, great care must be taken to put a proper support back of the knee, under the popliteal space, for extreme extension of the leg, without this support, may cause muscular spasm and severe pain: and at times it will be imperatively necessary to avoid extreme extension of the leg.

In order to reduce the fragments, it is, therefore, necessary for the surgeon to extend the leg of his patient; to reflex the thigh, by raising it or by putting the body toward a sitting posture; to

support the limb on a posterior splint; to apply direct pressure to the fragments. These indications have been met by various appliances invented by different surgeons. It will be interesting and instructive to trace, in a brief manner, the evolution of these appliances down to the time of their transformation into the more practical apparatus of the present. In doing this I shall make use of the researches of Malgaigne: Some of the earlier surgeons do not even mention fractures of the patella. Paulus Ægineta and Paré kept the leg extended with splints, straw-compresses, or troughs. T. L. Petit put the leg on a pillow raised toward the foot. Valentin, in 1772, extended the inclined plane, made of pillows, from the leg, under the thigh: at the same time he put a slipper on the foot and attached it to a body-piece around the chest. Richerand used the inclined plane, made of pillows, and left off the slipper. Sebatier increased the flexion of the thigh, and bent the knee slightly to relieve spasm and pain. Sheldon, in 1789, advised that the patient should sit up in bed, or even lean forward, in order to relax the rectus femoris. Albucasis kept a splint perforated in the center upon the front of the knee by means of a bandage. Purmann made and used a ring of twisted iron wire, having a double covering of leather. Meibomius modelled a little hat—*petit chapeau*—having a wide brim, on the sound patella, and stuffed it with cotton. Kaltschmidt made a wooden cap, doubtless in imitation of the "*petit chapeau*." Muschenbrök, a mechanic of Leyden, devised an apparatus that acted by parallel pressure. Arnaud modified this apparatus and gave it his own name. "It consisted of a trough of sheet-iron or tin, placed beneath the ham, and provided with a fenestra so that this part might be moistened if necessary, and having holes cut for screws along the lateral margin. Two wide concave plates, with holes corresponding to these, were applied one above the other below the patella and fastened by means of screws passed through the holes above mentioned." (See Packard's *Malgaigne*.)

The principle of the apparatus devised by the Leyden mechanic has been variously modified by surgeons since the time of Arnaud. Seyers' apparatus consisted of a hollow wooden splint, into which the limb was laid, and from which straps were carried over the knee so as to draw the upper fragment down and the lower one up. Velpeau's figure-of-8 apparatus involved a similar principle of reduction and retention of the patellar fragments. Sir Astley Cooper's

apparatus was somewhat different: The limb was bandaged from the toes to the knee, above which was applied a circular bandage which was brought downward by longitudinal tapes, fastened to the bandage on the leg. Dorsey's patella splint was applied to the posterior surface of the limb, and had two straps which passed obliquely across the knee, above and below, in such a manner as to support the lower fragment and pull the upper one down. Lansdale's apparatus consists of a posterior trough-splint, from which two loops of metal pass around the limb above and below the knee, and through whose arches there are thumb-screws for pressing upon pads, resting on the integument over the fragments.

Hamilton's apparatus consists of a posterior splint, flat or trough-like, upon which the limb is placed, and around which bandages are so passed in front as to raise the lower fragment and bring down the upper one: and at times he employs a foot-piece. Agnew's apparatus is made of a piece of pine board, bevelled at the ends, and having two pegs inserted on each side, from which bandages are carried around in front of the knee, in an oblique manner, so as to reduce and retain the fragments in place: the splint is applied to the back of the limb. Burge's apparatus ingeniously applies the principle of traction and counter-traction to the posterior patella-splint by means of pulleys and weights, two of which draw up the lower fragment, and the other two draw the upper fragment down. Malgaigne's apparatus consists of two metallic pieces, to which are attached four hooks, two above and two below; the lower hooks penetrate the lower fragment, and the upper hooks penetrate the upper one; a long thumb-screw draws the hooks together, reducing and retaining the fragments in place. A number of surgeons have applied an apparatus made of plaster-of-Paris in the treatment of fractures of the patella: It combines the posterior splint and the ring of Albucasis. The ring is a fenestrum left in the part of the posterior splint that is carried around in front of the knee-joint.

Wight's apparatus has a bed-piece and an upright piece joined at a right angle: to the bed-piece are hinged two movable bars, on which is fastened a hammock of canvas for supporting the injured limb with the foot elevated; a broad piece of adhesive plaster is bandaged to the front of the thigh, so as to embrace the upper fragment, and draw it down by means of weights and cords over pulleys on the upright piece; the lower fragment is kept reduced by a small

sand-bag, a bandage, or adhesive plaster. This apparatus permits the patient to move about while he is in bed, and yet keeps the fragments well reduced all the time. It affords the patient the maximum of relief, ease and comfort, and gives as good results as can be obtained by any one of the great number of inventions devised by surgeons for treating fractures of the patella.

Finally, it may be said that Desault was probably the first surgeon who employed the posterior splint for treating fractures of the patella, notwithstanding the claims of Arnaud and the mechanic, whose apparatus he copied and modified.

It must be of interest and value to know how distinguished surgeons have met difficult practical problems, such as fracture of the patella. And, to this end, I have made the following condensed statements. Hamilton's practice: The posterior splint is made of leather, gum shellac cloth or other suitable material, extending from two or three inches above the heel to a point beyond the middle of the thigh, and embracing about one-half the circumference of the limb, to which it is moulded and dried, and then padded and covered with a cloth sack. The foot is elevated six or eight inches, and a suitable pad put in the popliteal space, when the splint is applied by means of three bandages: one is put on from below upward to a point three inches below the knee; another begins three inches above the knee and goes to the upper end of the splint; the last bandage is one for reduction and retention; it is passed obliquely upward and downward around the knee, while an assistant presses down the upper fragment, and its final turns go in a circular direction around the patella. No pads are applied over the fragments. On the second or third day the bandage is tightened by overstretching, as there will be less swelling. At the end of about four weeks the bandage should be removed. Then the knee will be quite stiff. The surgeon may make very gentle passive motion, while an assistant presses downward on the upper fragment. He should be very careful not to rupture the intervening ligament, and substitute an ununited patella for an ankylosed joint. Daily after this the passive motion may be repeated, and in the meantime the patient, if he chooses, may be got up on crutches. In six or eight weeks the bond of union is quite complete; but there is danger of the new ligament being ruptured, —and this danger will exist for several months. For quite a long time the patient will have to wear a short posterior splint to guard

sudden bending of the knee, in order to prevent a rupture of the new bond of union. This splint can be made by cutting down the splint that was for the fracture in the first place. "Under no circumstances," says Hamilton, "is the surgeon justified in attempting to overcome the ankylosis by force, either with or without an anesthetic." And he subsequently adds: "In time, and generally within a year or two, the ankylosis will disappear under careful and moderate use of the limb."

Hitherto we have not obtained bony union, except in rare instances. We can only hope to obtain ligamentous union: this is the rule. From time to time we obtain no union at all, a result more frequent than bony union. These points are well established, and cannot be controverted. By long confinement, with immobility of the knee-joint, whose patella has been broken, serious and maybe incurable ankylosis may occur. To break up this ankylosis involves the rupture of the new ligamentous bond between the fragments, and no judicious surgeon will undertake it: yet something to this effect may be done in the course of a year or two. The stiffness of the knee-joint may continue for years, and it may never be removed. It is impossible to make early passive motion of the knee-joint without disturbing the new union of the fragments, either causing elongation of the ligament or producing non-union altogether. The disability of ankylosis results on one hand, and on the other that of imperfect union may occur. And hence in whatever way we look and act, we are met by great practical difficulties. Surgeons, recognizing these difficulties, have endeavored to meet them as best they could, some in one way, and some in another; one has preferred a stiff knee with firm union of the patellar fragments; another has preferred a movable knee with such union as he could obtain under the circumstances; and a third has tried to obtain as firm union as possible, accompanied by the greatest degree of motion in the knee-joint. These three lines of practice were formerly carried out by the French surgeons: one would put the limb into an immovable apparatus until the fragments united; one putting the limb at rest, but moving the knee-joint; and a third applying some apparatus and at the same time making more or less passive motion.

Among English surgeons we find that there have been also three lines of practice: one relies "simply on the position of the limb."

And here we may give what seems to be the reason of this practice. To illustrate:

CASE XLVII.—A man, 23 years of age, broke his left patella the day previous; three weeks before he knocked his knee forcibly against a hard body; he had walked about in the meantime: at the time of the second accident he was walking up an incline, when he slipped, and tried to save himself from falling; he came with his entire weight on the left leg, when the patella broke transversely below the middle and went down. In the first place, the patella was incompletely broken or bruised, so that the quadriceps could produce a fracture under the circumstances related; the knee was swollen and hard; the leg could not be raised by volition; the patient could walk on the level with a slight limp, both forward and backward; the upper fragment kept its place quite firmly; and the voluntary force of the quadriceps seemed to be much less than normal. And then two points are suggestive: In some cases the upper fragment, after a certain length of time, is kept by its anatomical connections from any further displacement that is material; nor does the quadriceps contract forcibly, either by volition or irritation; and in the meantime the leg is at rest, so that the knee is not bent: a bond of union is formed, much the same as we get in a case of tenotomy. The fracture has been treated by position; there has been some motion of the knee; the patient has been confined only a few weeks; a stiff joint has been prevented; a good tendinous band has been formed between the fragments; and the disability is not very great. Yet all cases are not like this one.

Another line of practice consists in applying some apparatus immediately after the accident for the purpose of reducing and keeping the fragments in place. We may refer the reader to our statement of the practice of Hamilton, who is an advocate of this plan. Perhaps the majority of surgeons in more recent times have been in favor of applying some kind of apparatus immediately after the patella has been broken.

In the third plan of treatment the retentive apparatus is not applied till some days have elapsed after the accident. The advice is to wait for the absorption of the effused blood and for the subsidence of the swelling. This generally takes some ten or fourteen days. Then the fragments can be reached, and reduced, and kept in place by the retentive apparatus, much the same as if it had been

applied in a case that had no swelling in the outset. But it must be remarked that, in the meantime, the upper fragment will have a greater displacement, and adhesions will have formed in the injured tissues. So it must follow that reduction cannot be so complete at the end of 14 days as it would be just after the accident.

Upon reflection it will be seen that fractures of the patella may be at first arranged into two classes: (1) In which the effusion and swelling are slight or only moderate; and (2) in which the effusion and swelling are considerable or extensive. Practically all cases may be put in one or the other of these two classes; it may require experience to draw the line between them. In the first class we may apply an apparatus at once; in the second class, for reasons above given, we may wait a few days for reduction and retention. And then the first class may be subdivided: in one set of cases there is more or less separation of the fragments, which ought to be reduced at once and kept in place by some apparatus; in the other, and they are few, there may be little or no displacement of the fragments, which unite better if they are not left to themselves, as they must be when the case is treated simply by position.

There can be no question about the disability which may follow the treatment of fracture of the patella by means of any apparatus. Bayer knew several persons in Paris who were obliged to wear a contrivance to hinder the leg from bending at the knee. It may be necessary to use a cane or crutch in walking. Cases occur in which the power to extend the leg in walking has never been restored. John Hunter and Sir Astley Cooper have quoted such cases; they have also mentioned cases in which the power of extending the leg has been entirely lost. Under such circumstances, the patient may throw the weight of the body on the uninjured limb, and break the sound patella. Surgeons have quite frequently observed the occurrence of this accident. But the rupture of the new bond of union has been more common, and has quite often been attended by serious results. Sir Charles Bell reports a case of refracture of the patella in which the skin was torn, on account of the patient falling backward, and the compound injury made it necessary to amputate the limb. Malgaigne says: "I have seen a nearly similar case; the rupture of the fibrous band was attended with enormous ecchymosis, gangrene ensued about the fifth day, and death closed the scene." Then he adds: "M. Seutin sought in vain to save a limb thus affected;

after four months of suffering, amputation of the thigh became the only resource."

In Hamilton's treatise on Fractures and Dislocations we find some important evidence in regard to the result after fractures of the patella. The ankylosis has generally disappeared under passive and active use within a year or two. But the new ligament gave way more or less completely in 27 cases out of 127. Of this last number of cases there were 5 which had the opposite patella broken. A soldier had no union and a separation of the fragments to the extent of 5 inches, and was unable to walk well at the end of 29 years. A case in which, after 4 years, there was a separation of the fragments as great as 4 inches, walked badly. And the author had not seen bony union in any case. A man, 38 years of age, had an old fracture of the patella, and the fragments were separated nearly 4 inches, there being no apparent bond of union; and he was unable to make voluntary extension of the leg. A soldier, 29 years after breaking his patella, had no trace of any kind of union of the fragments, and, while he could walk without a cane, he had some limp and could not go fast. A laborer, 17 years after breaking his patella, had the fragments separated nearly 4 inches, without any bond of union. "He cannot extend the leg by muscular action when sitting, but he can flex it to an acute angle with the thigh. Standing he can flex and extend it perfectly. In extending he turns the foot out, in order to bring into action the outer portion of the quadriceps. He has always, since this accident, been somewhat lame, but could walk several miles, and carry loads without a cane."

These distinguished witnesses have been summoned to testify in regard to the worst cases and the most unfortunate results: and these cases are not rare. Indeed, we have not the kind of statistics to enable us to fix the average disability following fractures of the patella. But we can truly say that there is extensive peril, as well as great disability, connected with quite a number of these fractures. This part of the evidence must stand without the possibility of contradiction. On the other hand, the greater number of cases have a recovery which surgeons have been in the habit of calling good. But, in estimating the disability following fracture of the patella, there is one source of error which has been overlooked, and for which surgeons may be excused. The question of treatment has been difficult; the results have not been as good as we could expect; the obstacles

in some cases have been insuperable; and so one surgeon after another has devised a new apparatus, which he has desired to overcome every obstruction; he may honestly think he has succeeded better than any one else; he extols his plan and gives and magnifies the results; and what he has said and written may perhaps be better than the facts described. So that, even in the more fortunate cases, there has been some disability that has remained permanent, or for a long time after the two years generally required for regaining the use of the limb. The reason for this delay and for this permanency in the results may be expressed as follows:

When a joint is seriously diseased or injured, the muscles that move it atrophy, not only from disuse and immobility, but also from disturbance of the dynamic relations. The bones, the nerves, and the muscles of a joint bear to each other the relations of impression, contraction, and motion, and if there is a disturbance anywhere in the circle, the power will suffer. This change may be seen in various parts of the body, and is amply illustrated by cases of fracture and dislocation. The enforced rest of the patient, as well as the pressure of the apparatus, contributes to the increase of the disturbance. Then this atrophy continues a long time, even after such recovery as the surgeon is able to obtain; and this may not be until two years have elapsed. There may be a weak union or a long ligament, or a non-union, leaving a sense of disability, a feeling of want of power, an impairment of confidence, and the quadriceps continues its atrophy, not being called upon to do full work. And what is more, the mechanical relations are changed. In place of the broad and firm support by means of the patella, we have such only as can be afforded by a ligamentous hand. If the tendon of the quadriceps had been all that was needed, the patella would not have been provided, nor would surgeons have been so anxious to get bony union of its fragments. Yet, in many instances, while the voluntary motion of the knee-joint may be restored, there remain some loss of confidence and some disability. In the main the quadriceps is not apt to regain its full power, the strength of the limb is diminished, and the capacity of the patient to work is not so great as it was before the injury.

But it must be kept in mind that anything which limits the movement of the knee-joint produces disability, and this, implied by the fact that a knee-cap must be worn, not only to prevent a con-

secutive, but also a refracture of the patella. That a refracture of the bond of union is serious and often leads to great disability is well shown by some observations of Hamilton. A permanent reunion was not effected in any case of refracture in which the second injury took place later than three months subsequent to the first: these became cases of non-union, and there were about twelve of them. As many more cases, which were refractured before three months from the time of the original accident had elapsed, terminated very satisfactorily. But three others were not so fortunate. These cases are related in a report of some special investigations of fractures of the patella by Hamilton. He adds: A majority of these cases refuse to unite again, even by fibrous tissue, whatever means may be employed; and the few cases of success which have come to my knowledge are confined almost entirely to those examples in which the rupture took place soon after the apparatus was removed, and in which the limb was immediately subjected to treatment. When the fragments do unite, the patients are for a long time seriously maimed, the limb lacks stability and often gives way suddenly under the weight of the body.

Some points in regard to the mechanics of the knee-joint may be considered more in detail. The posterior surface of the patella has an extent of from two to four square inches. Now, in order to raise the weight of an average-sized man, under ordinary conditions, with the quadriceps extensor and the femoral lever, the patella will press on the condyles with a force anywhere from 500 to 1500 pounds avoirdupois. But when the body supports a weight or acquires considerable momentum, or when one is going upstairs, the pressure of the patella will greatly exceed this estimate. On the basis of these facts we can readily see the importance of the patella in the act of locomotion, especially in going up and down stairs, for, if we suppose it to be very much smaller than it is, or that the tendon of the quadriceps had no sesamoid bone, we would have undue pressure at one point, or in one line, on the femoral condyles, and the effect at times might be some structural change, when, as we know, a cubic inch of cancellous bone will only sustain a pressure of about 600 pounds avoirdupois. As a corroborating fact, we may mention that the patella is sometimes turned on its edge—a kind of dislocation, and by the power of the quadriceps forced so firmly into the cancellous tissue of the condyles as to prevent its being detached and

reduced. So it may be a fortunate circumstance that the quadriceps becomes atrophied and weakened,—for it would seem to be adjusted to its new dynamic relations. In other words, when power is not required, or when it would do injury, it is not supplied.

There is an important pathologic fact, which I have verified when I have wired the patella fragments together; that is, the upper fragment may be attached to the femoral condyles by strong adhesions, which will limit the motions of the leg; this fragment will not move downward and will arrest the flexion of the leg; and it may be that the ligamentous union will be so elongated that the quadriceps may not act upon it to any material extent; and hence, if the adhesions are stronger than the bond of union, it is apparent that forcible passive motion will be the cause of a refracture. The limited contraction of the quadriceps stands in the way of its regaining power,—and so we have other reasons for the disability following fracture of the patella.

The operation of opening the knee-joint for the purpose of wiring the fragments of the fractured patella was performed by Rhea Barton in 1834, by McClellan in 1838, by Cooper in 1861, by Logan and Gunn subsequently, by Camedon in 1877, by Holmes in 1880, by Lauenstein in 1882, by Sir Joseph Lister in 1882, and by a large number of surgeons since that time. This operation was first performed by American surgeons. It was revived forty years after in Scotland. In England it received a great impetus, and it now has a permanent place among surgical procedures.

Compound fractures usually come to us with the joint infected, and an aseptic operation is the only course open.

Poland collected 69 cases of compound fracture of the patella: amputation was performed in 7; 18 of them died; and 44 recovered with the following results: some impairment of the functions of the joint was left in 17, of which only 3 suppurated; in 11 the joint had limited motion; there was complete ankylosis in 16, in several of which there was profuse suppuration, as well as danger to life. The disability, as well as the death-rate, shown by these statistics, other things being equal, can no doubt be diminished in the future, not only by antiseptic practice, but also by wiring the fragments. The severity of the injuries in any case has much to do with the result. A series of severe injuries would give a higher death-rate and an average of greater disability. Then the constitu-

tion and health of the patient affect the result of an injury. One of vigorous health might have a good recovery, while another with a broken constitution might die.

Age, also, as every one knows, is an important factor in estimating the results of serious injuries, such as a compound fracture of the patella. Antisepsis is of the utmost importance in injuries of and operations on the joints. For antisepsis may give us life, where a fatal issue would have occurred without it. It can also give us motion in a joint in the place of ankylosis—that would follow under other plans of treatment. To bring the broken surfaces of bony fragments into close contact and hold them there, diminishes the work of repair, accelerates the recovery, decreases the death-rate, and lessens the disability,—especially under the influence of antiseptics. The repair that takes place between bony fragments in close apposition is similar to the primary union of soft parts: new bone is formed in almost every instance.

In October, 1883, Sir Joseph Lister, when asked his reasons for wiring the patellar fragments, replied to the London Medical Society in effect: Because it relieves spasm of the quadriceps extensor and allows the blood to escape from the joint. When it was alleged that aspiration would remove the blood, and that tenotomy would relieve the spasm, his answer was, *that he had faith in his antisepsis*. And, as we know, it is careful antiseptic practice that makes this operation possible and successful.

At the outset, let us state the possible advantages of this operation: the fragments grow together by bone, the union being quite firm at the end of a week or ten days; the patient is kept in bed only four or five weeks, and then gets up and walks about; the motions of the knee-joint are generally restored in a short time, sometimes in two or three months; the strength of the limb is regained, so that there is only slight disability, or none at all; the distress and discomfort of the patient are much less than under the usual plans of treatment; and this implies that the operation is properly performed.

The following rules may be observed:

(1) The most careful and perfect asepsis should be practised at every step of the operation.

(2) In both the primary and secondary accidents the patient must be prepared for the operation, which, as a rule, is best per-

formed at the end of the tenth or fourteenth day subsequent to the date of the fracture. Here we may state the reasons: recently injured tissues do not act as well, when operated upon, as those that are more normal—a fact known by experience; the effused blood can be absorbed during this time or it can be removed by aspiration; the general condition of the patient will be improved by rest and other treatment.

(3) A longitudinal incision may be used and should be just long enough to permit the subsequent steps of the operation, or a flap may be turned up.

(4) The broken ends of the fragments must be sawed off evenly, so that they will come together accurately and restore the original form of the patella as far as can be.

(5) From the origin of the ligamentum patellæ drill a hole through the lower fragment obliquely backward and upward to the edge of its articular surface, from the insertion of the tendo-patellæ also drill a hole through the upper fragment obliquely backward and downward to the edge of its articular surface. In instances of great tension, partly relieved by tenotomy, drill a hole transversely at the lateral borders of each fragment, secure the wire by twisting, bring the fragments together and twist the opposing free ends of the wire.

(6) The prepatellar fibrous tissue is brought together with chromicized catgut or kangaroo tendon applied after the manner of Billroth's bundle suture.

(7) The eye end of a strong needle, armed with silk and passed through the holes, is again withdrawn, carrying with it the silver-wire bone sutures.

(8) The wound is sutured and drained if necessary. The limb is placed on a posterior splint and elevated in bed. After three weeks a lighter splint is applied, and he is allowed to get up on crutches.

The causes of failure in wiring the patella are:

- (1) Inability to bring the fragments together.
- (2) Septic conditions.
- (3) Necrosis of the fragment.
- (4) Diathetic conditions.
- (5) Age and osteoporosis.

BIBLIOGRAPHY.

- Wight, Records of cases and publications.
Marcy, of Boston, Personal Letters.
Dennis, New York Med. Journ., April 3 and 10, 1886.
Turner, Clinc. Soc. Trans., vol. xviii, p. 41.
Jacobson and Steward, The Operations of Surgery.
Macewen, Lancet, November 17, 1883.
Ann. of Surgery, March, 1887, p. 178.
Fowler, Ann. of Surgery, September, 1885, p. 248.
Powers, Ann. of Surgery, July, 1898, p. 67.
Ward, Lancet, November 1, 1884.
Turner, Lancet, 1887, vol. i, p. 572.
Wheelhouse, Brit. Med. Journ., June 9, 1883.
Teale, Brit. Med. Journ., June 9, 1883.
Turner, Table of cases, Lancet, 1883.

PARAFFINE INJECTIONS BY THE "COLD" PROCESS

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IN March of last year M. Lagarde read before the Paris Academy of Medicine a paper that attracted a good deal of attention, concerning an instrument designed to facilitate interstitial injections of paraffine. With this new syringe the softening of paraffine can be effected by mechanical means, which enables injections to be made no longer heated, but at the surrounding temperature. To this end the piston is mounted on a rod provided with a screw-thread, and by a slow and gradual screw movement the piston advances, pressing against the paraffine, which finally issues from the end of the cannula in the shape of a doughy thread. M. Lagarde adapted to the body of the syringe a fixed handle at right angles, which enables the instrument to be firmly held during the operation.

Other syringes, practically identical, and for the same purpose, were invented at the same time, so to speak, by Stein, of Wiesbaden; Gersuny, of Vienna, and before them, even, by Harmon Smith and Gregory Connell, two American physicians. But these different instruments were really only reproductions of the old screw syringe, and particularly of Guyon's instrument.

The phenomenon of driving out, in a condition of paste, at one end of the barrel of a syringe, paraffine, put into the other end of the barrel in a solid form, is certainly a very curious one, but easy to understand, if we have at our disposal sufficient propulsive power to drive the piston pressing on the paraffine; it would even reduce it to a liquid, if the paraffine could find no way out.

With a suitable instrument based on this principle, all the drawbacks sometimes connected with the heated paraffine injections would at once be abolished, such as burns, escape of the paraffine into the surrounding tissues, thrombophlebitis, etc. And particularly for submucous injections, and for restoring atrophied turbinate bones, would this injection of cold paraffine be of the greatest importance. However, it must be admitted that the syringes fashioned according

to Lagarde, Stein, and Gersuny do not fulfil the desired purpose. Their weak point is that they require the use of both hands, and whatever may be the operator's skill, he cannot possibly under such conditions succeed with so delicate an operation.

For this reason I resolved to try to overcome this difficulty, as otherwise the method did not seem to me practical, but rather likely to disappear. I therefore began by having made a syringe somewhat handier than the preceding ones, to which I adapted a cannula specially suited for intranasal injections. As I showed at the meeting of the Belgian Oto-Laryngologists, last June, this instrument works with the greatest facility, though it was subject to the same criticism as that made concerning the other syringes; but on that occasion I remarked that it seemed to me possible either to fasten this syringe on the handle of an electric motor or on a lever-forceps: the power developed in this way might be found sufficient to drive the piston forward and bring the necessary pressure to bear on the paraffine.

After a number of experiments I finally found myself in possession of an instrument enabling me to inject cold paraffine with the use of a single hand; but the instrument that I presented at the last international meeting of otologists, held at Bordeaux, in last August, seemed to me still somewhat clumsy and not sufficiently handy. There then remained merely the reduction of the capacity of the syringe barrel, and the decrease in the dimensions of the other parts of the apparatus, to do away with their twofold defect.

The instrument I am about to describe is my latest one, which has already been used in a relatively large number of cases.

As will be seen from the drawing of this instrument (Fig. 1), it is composed of two distinct parts: (1) A metallic syringe, with a metal piston fitted with a rack; and (2) a syringe-forceps, that drives the piston.

(1) *The Syringe*.—The barrel, with thick metal walls, is nine centimeters long. Its capacity is hardly more than one good cubic centimeter, as its inner diameter is very small, which admits of exerting great pressure within the barrel. Both ends are fitted with screw-threads: one, the more pointed, is designed to hold the cannula; the other fits onto the forceps that is to drive the piston. The cannulæ, which are of various sizes, have either the shape of a bayonet, are straight, or curved; their caliber is fairly large, except

the end, which is smaller, slightly flattened and bevelled. The piston is formed of a metallic rod fitted with a rack; it is 11.5 centimeters long, and there are fifteen cogs.

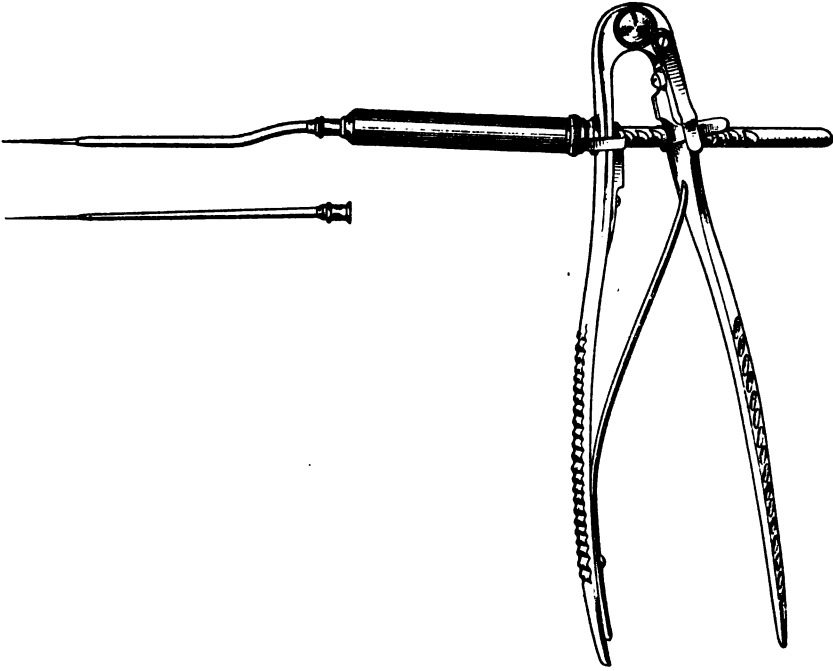


FIG. 1.—Dr. Broeckaert's automatic lever syringe for submucous injections of solid paraffine.

(2) *The Forceps*.—This is a lever of the second variety, composed of two arms 20 centimeters in length; it is fitted with a spring and can be taken to pieces. To the anterior, or fixed arm, is adapted a small spring click, which rises as the piston advances and catches in the cogs to allow the movable arm to go backward. A similar click, fitted with a spring, is fastened to the movable arm, and serves to catch in the notches to drive the piston forward, and to throw itself out of gear while a new notch is seized.

To use the instrument, the barrel is filled by inserting a small cylinder of sterilized paraffine that melts at 45° C. and has been kept in a tube hermetically closed at both ends. This little operation should be done by pushing with a glass rod the cylinder of paraffine from the tube directly into the syringe, into which a drop of liquid vaseline has been allowed to fall. A sterilized cannula is then screwed to one end of the syringe, which in turn is screwed to

the fixed arm of the forceps. The piston is then passed through the oval opening of the movable arm of the forceps until it reaches the interior of the syringe, while with the left hand the spring click is raised. Finally, the little click is brought in contact with the clogged side of the piston, and kept in place by means of a spring.

The apparatus is now ready for use; the two branches of the forceps have only to be taken in the hand and pressure brought to bear for the forceps to advance. When the spring click of the fixed arm is caught in a notch the two arms should be separated gradually until a slight metallic snap indicates that another cog has been caught, and that it is now possible again to push the rack-piston forward. The piston is, therefore, made to progress by alternately opening and closing the forceps, and the paraffine appears at the extremity of the cannula in the form of a thread that can be readily moulded with the fingers.

In order to facilitate the issue of the paraffine it may be useful to warm the cannula lightly by holding it a moment in the hand; in this way the paraffine at the very end of the cannula is softened, and nothing is required beyond a moderate, though steady, pressure to obtain the effect desired.

The technic for the restoration of atrophied turbinate bones is as follows: After carefully freeing the nasal fossa from the crusts and secretions it contains, the septum and inferior turbinate should be painted with a solution of cocain. It is advantageous to limit this application to the anterior half of the bone, in order to leave the posterior portion in a turgescient condition, which considerably facilitates the introduction of the cannula.

The entrance to the nasal fossa should be held wide open by means of a large speculum in the left hand. The forceps carrying the syringe should then be taken with the right hand, and the point of the cannula inserted into the submucous space, at the most suitable spot, which is the one where the mucous membrane seems least atrophied. The injection is then made slowly and without jerks. Little by little the turbinate is seen to swell from in front backward, grow pale in color, and assume dimensions more or less increased.

At the first treatment it is well to be satisfied with reforming the posterior portion of the lower turbinate; in a further series of treatments these bones can be entirely restored. There is no real objec-

tion to proceeding at once, after the initial injection, to make others, by introducing the cannula at suitably selected spots.

There is nothing easier than to create by means of a paraffine injection an artificial spur by injecting beneath the mucous membrane of the septum, such as that of the floor of the nasal fossa, a certain amount of that substance.

It is much more frequent for a "cold" injection to succeed than for a hot one, for the reason that we are now no longer obliged to act with the great celerity that was formerly necessary to avoid the paraffine solidifying in the cannula and refusing to flow any longer. By using this new syringe we can act with deliberation, and place the paraffine where and how we wish, without its exerting any too great pressure and tearing a mucous membrane that may be very fragile.

We must, however, not lay undue stress on the facility of the technic; in this case, as in all delicate operations, practice and patience are required, and only by passing through a series of unsuccessful attempts can the dexterity for this kind of operation be acquired. I advise beginners first to familiarize themselves with the working of the apparatus, and then to select their cases; that is to say, to choose docile adults whose turbinates are only moderately atrophied. In this way they will be more likely to succeed with the method, and avoid disappointments.

I have had no mishaps nor complications worthy of mention since I began with the "cold" injections. The operation itself is generally not painful, though in some instances the patients speak of severe pain in the cornu of the eye, or even in the roots of the teeth, at the time of the operation. This pain, however, rarely lasts more than a few minutes. Some patients complain of headache; but this symptom is much more ephemeral than when the hot injections were used. Signs of irritation are reduced to a minimum; only in exceptional cases have I seen any edema, and even then it was very limited and fugacious.

Setting aside accidents that might occur through defective anti-sepsis, I feel that when this method is well applied it is absolutely harmless. Whereas formerly the percentage of cases of facial phlebitis was fairly high, the present perfected technic makes the risk of such mishaps almost nil.

It goes without saying that my operations are still too recent to

warrant me holding any definite opinion as to the curative value of the two methods of interstitial injections of paraffine in the treatment of fetid atrophic catarrh; the results obtained must first stand the test of time. But what I am already in a position to say is that the number of cases in which it is possible to restore a normal caliber to a nose has considerably increased with the "cold" injection method. Now, it is beyond question that a narrowing of the dimensions of a nasal fossa produces marked improvement in all the signs of ozena. I am, therefore, convinced that the new method will soon be able to point to results more numerous and at least as satisfactory as the original method. Why should it be otherwise, since we know that 45° paraffine, introduced beneath the nasal mucous membrane, sets up a regenerative process due to stimulation of the phagocytes that penetrate into the interior of the foreign mass? I hope soon to have occasion to show the histologic transformations that take place in the atrophied mucous membrane after a "cold" injection of paraffine; removal of portions of membrane treated will enable me to examine this point.

In the present article it is not my purpose to show to what extent the method of submucous injections of paraffine is able to improve or cure atrophic catarrh. If I rely on my personal experience,—which dates from the commencement of 1902 and is based on a number of cases that is already considerable,—and on the testimony of writers who have tried this means of treatment, I can say, though, that no other method is comparable to it.

Moore published last year statistics based on 70 cases taken as they chanced to come to his clinic; they gave 62 per cent. of recoveries and 33 per cent. of improvements. By cases improved he says that he means suppression of the odor and crusts; but since viscid matter continued to be secreted he considered that recovery was not complete.

Baratoux, who has also used these injections for a long time in the treatment of atrophic rhinitis, concludes, in an article recently published, that the curative action of paraffine injections in ozena is far from problematical, and that the curability of this disorder is demonstrated.

Personally, I have published on several occasions the results of my experience, which is similar to that of all who have written on the subject.

Among the most fervent adepts of the method can be mentioned: Helmsœrtel, de Stella, Delie, Tretop, in Belgium; Compaired and Botey, in Spain; Fliess, in Germany; Lake, in England, and Zaalberg, in Holland. All of these writers have used the method frequently, and consider the immediate and remote results very encouraging and infinitely superior to any given by the former treatments. I am convinced that from now on this new and simplified treatment will make fresh and earnest proselytes, who will successfully overcome the tenacious disorder known as fetid atrophic rhinitis.

I still wish to make a few remarks about the use of "cold" paraffine injections as a means of prothesis, either for esthetic purposes, in correcting certain congenital or acquired deformities, or for obturating natural or accidental orifices.

The instrument described by me above is only of use for *submucous* injections, in which 45° paraffine is the heat substance to be employed.

For external corrections, and particularly for nasal prothesis, it is preferable in most cases to use paraffine whose point of fusion is nearer 50°. But for this we should have to resort to a far greater propulsive power, and to modify the size and shape of the instrument. To turn this difficulty, M. Lagarde advises that the syringe when charged should be dipped in water at about the temperature of the fusing-point of the paraffine employed. A few minutes' immersion suffices to soften up the substance to a certain degree, enabling it to be used in a pasty state, as one would a 45° paraffine.

However this may be, there is up to the present time no form of syringe that can be looked on as a practical instrument for this kind of operation. I hope, however, to succeed in my attempts, and that the new syringe, whose mechanism I am now studying, may be able to replace with advantage the older one in certain cases of external prothesis.

It would indeed be a mistake to effect all prothesis by the "cold" process, unless we could find some apparatus with such a degree of pressure that the paraffine would come out in a liquid state and not in the form of a flexible thread. It is only in exceptional cases, and in dealing with unimportant deformities, that the "cold" process is indicated. Even in such instances I am afraid that the paraffine will not lend itself to modelling with sufficient readiness to give a

really esthetic result. For when a liquid mass has been injected, which only solidifies after a certain lapse of time, the region can be kneaded at will, and not only a satisfactory shape given to it, but an artistic contour striven for.

The objection can be made that prosthesis by means of liquefied paraffine may entail serious drawbacks, or even be dangerous in some instances. It is true that injections of vaseline, and even of paraffine, have entailed accidents in the hands of operators not sufficiently familiar with the delicate technic of the process; but I feel confident in asserting that, as far as nasal prosthesis is concerned, no serious complication need be apprehended when the injection is made in accordance with the precepts to which I have a number of times called attention. The rather unique experience that I possess of this method enables me to be quite affirmative concerning its harmlessness. For I have made hundreds of injections of solid paraffine since the month of November, 1901, not only for utilitarian purposes, but in many cases in which esthetics and looks alone were under consideration. If I do not take into account a few operative accidents of small importance, due to my lack of experience at the beginning, I can say that prosthesis by paraffine injections in cases of nasal deformity is absolutely free from all danger; a skilful and experienced operator can always guarantee his result in such instances, both as regards appearances and the future outlook.

It would be easy to show that all the mishaps that have been laid to the method are due to nothing save the operator's clumsiness. Usually the trouble is due to the escape of the liquid paraffine out of the region whose appearance is to be improved. Thus, some operators have published cases in which the paraffine, instead of solidifying in front of the nasal depression, had fused to the sides and formed a voluminous lump on either hand of it. Others have reported, after such injections, tumors of the lids, forehead, and folds between the nose and cheek. I have more than once been called on to remedy such a state of affairs, and in each instance have found that the tumors were nothing but lumps of paraffine that had escaped from the region where it was intended to remain. In cases fortunately altogether exceptional, blindness has been reported, attributed to thrombosis of the ophthalmic vein; I think, however, that such accidents must be due to diffusion of the paraffine into the orbit, and not to penetration of this substance into a vein. The

latter accident is rendered impossible by making the puncture with the cannula before filling the syringe.

More recently still, attempts have been made to show that these injections are far from being as harmless as might be supposed, as they may give rise to trophic and circulatory disorders of the skin. This mistake arose from the fact that in certain medical publications this possibility was attributed to all paraffine injections, whereas it had occurred after injections into the breast of a mixture of low-fusion-point paraffine and vaseline. I am not at all in favor of such operative measures as the latter, which are done for pure coquetry and are most uncertain as to their results. It is not surprising that operators who use these injections for anything and everything, who with their poisons do not hesitate to fill up the supra- and sub-clavicular or supra-sternal spaces, as well as other dangerous regions, necessarily render themselves liable to failure, if not disaster, and such excesses in the use of the method cannot be too severely criticised.

The difficulties encountered in endeavoring to inject paraffine into firm and resisting cicatricial tissue, when there are no interstices in which it can lodge, are easy to group. But here again the method can be successfully applied if the adhesions are freed before the operation is attempted; I am accustomed always to prepare beforehand with the cannula a pocket in which the paraffine can be deposited, and this precaution is very useful. In those more difficult cases still, in which the skin of the nose is the seat of deep cicatrices, and in which all elasticity appears to be lost, results that are often surprising can still be obtained by performing nasal prothesis, consisting in the combination of an autoplasmic operation and the paraffine injections. I reported the details of this operation at the last congress at Bordeaux.

From these various remarks the conclusion to be drawn is that the paraffine-injection method is steadily gaining in practical interest; and in this way is verified the statement with which I ended one of my first publications on the subject: The paraffine-injection method is one of the most recent applications of modern surgery, and perhaps one of the most fertile in its applications.

ETHYL CHLORID: ITS VALUE AS A GENERAL ANESTHETIC

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THE career of ethyl chlorid as a general anesthetic has been almost as chequered as that of nitrous oxid, but it has now come to stay, and may be considered to have established a claim to a front place in the armamentarium of the anesthetist. Ethyl chlorid has taken upward of half a century, however, to establish its position and to gain the confidence of the medical and dental professions. In 1848 Heyfelder first employed the drug to induce general anesthesia in the human subject. For a number of years after ethyl chlorid remained almost entirely in disuetude, although several observers commented favorably on its value. B. W. Richardson experimented with it in 1867, and found it to be "a good and safe anesthetic," but his remarks do not seem to have attracted the notice of the profession.

Some writers state that both Clover and Snow commented favorably on ethyl chlorid, but this statement is erroneous, the mistake having arisen from the fact that they both used and reported on ethidene dichlorid ($C_2H_4Cl_2$), a very unstable and dangerous drug, which rapidly fell into the disrepute which it deserved. Clover himself, in 1880, published a note of 1877 cases of anesthesia obtained by means of this drug.

In the year 1895 Carlson, the Director of the Dental Institute at Gothenberg, showed that in certain cases in which local anesthesia of the gums was produced by the ethyl chlorid spray, the patient became quite unconscious. He rightly concluded that this was due to inhalation of the vaporized ethyl chlorid. Then, Thiesing and Billeter purposely employed it as a general anesthetic with good results. Soulier, of Lyons, and Lotheissen, of Innsbruck, followed their example, and during the next few years several thousand cases were recorded and favorably commented on in the Continental surgical and dental journals. The drug was

largely employed as a general anesthetic in the clinic of von Hacker at Innsbruck, and extensive procedures carried out painlessly while the patient was under its influence: Gastrostomies, colostomies, herniotomies, tenotomies, operations for piles, fistula in ano and cancer of the breast were included among these. In 1901 McCardie, of Birmingham, began to use the drug, and in March of that year published a series of cases with favorable comments on the anesthetic properties which it possessed.

This first drew attention to the matter in Great Britain. McCardie continued using the drug in suitable cases and published further papers in July, 1901, and April, 1903, while at about the same time the country was flooded with literature concerning two French proprietary preparations of ethyl chlorid known respectively as "Kelene" and "Somnoforme." Demonstrations of the properties of these substances were given throughout the country by various interested persons, lay and otherwise. There is no doubt that they did a great deal to attract attention to the value of what was really the drug essentially employed—ethyl chlorid. The interest of the dental profession was at once attracted and the market rapidly flooded with inhalers, suitable and unsuitable, for the administration of "volatile anesthetics." At the present moment the fact is becoming generally recognized in the United Kingdom that in ethyl chlorid, and in ethyl chlorid alone, we have an exceedingly valuable anesthetic. The fact has been fairly well established that no admixture of ethyl bromid or methyl chlorid is necessary or indeed desirable or advantageous. In an exhaustive article on the subject, published in 1904, Hewitt has firmly expressed his disapproval of such mixtures, basing his statements on material facts. All the best opinion at the present moment favors the employment of a pure preparation of ethyl chlorid, placed on the market under the same name.

CHEMICAL AND PHYSICAL CHARACTERS

Ethyl chlorid or chlorethyl, "salz-aether" (German), has a chemical formula of C_2H_5Cl . It is a colorless liquid of aromatic odor, sweetish taste, and neutral reaction. It volatilizes at ordinary temperatures without leaving a residue. It has a density of 0.92 at $0^\circ C.$; the density of its vapor, taking air at unity, is 2.3, and it boils at $12.5^\circ C.$

It is very combustible, burning with a green flame and setting free hydrochloric acid. As it is usually put in tubes holding from 50 to 60 c.c., it shows no tendency to decompose or undergo chemical change, even when exposed to light. Its purchase in bulk, in larger quantities than those named, is not to be recommended to any one but a skilled chemist accustomed to handling it, owing to its extreme volatility.

It possesses considerable solvent action on various substances, but has no more appreciable action on rubber apparatus than has sulphuric ether. It rapidly destroys vulcanite stopcocks, etc.

It is readily soluble in alcohol, but sparingly so in water. Although extremely volatile if a few cubic centimeters be decanted into a small test-tube of thick glass, no considerable amount will be lost if left uncovered for five or ten minutes in a room at about 70° C., but the tendency to ebullition is marked if a small particle of glass or metal be suddenly dropped into the tube.

PHYSIOLOGIC ACTION

In 1880 the Committee of the British Medical Association investigated the action of ethyl chlorid on rabbits and considered the results of their experiments very unpromising. The respiration of these animals stopped soon after the inhalation was begun, and general convulsions ensued, ending in death. The committee were so unfavorably impressed that they dismissed the drug as unworthy of further consideration.

We find no further observations until the year 1892, when, at the request of the then editor of the "Dental Cosmos," Professor H. C. Wood, of Philadelphia, an observer of world-wide reputation, assisted by Dr. Cerna, investigated the physiologic properties of this drug in order to determine whether it could be of any service in general anesthesia. They made no pretensions, however, to "a scientific study" of it. They concluded, *a priori*, that any effect which it might have on the human system would be of very brief duration owing to the extreme volatility of the drug, and stated that their conclusions were entirely confirmed by their experiments. Dogs were used, and the drug was exhibited in some cases by inhalation and others by instillation by means of a cannula in the jugular vein. It is not necessary to describe their experiments at length, but it is sufficient to say that from the practical

anesthetist's point of view their apparatus was very crude and the dose used excessive, so that the results obtained could scarcely be expected to be favorable. Nor were they. Full anesthesia was obtained in about 20 seconds and lasted for two minutes, but it was accompanied by an alarming fall of blood-pressure beginning at the very start of the inhalation. The effect on the respiration was to increase markedly its rapidity, to the extent of about 50 per cent. These two results, together with what these observers termed the "fugacious" character of the anesthesia obtained by means of the drug, induced them to condemn it as not suited for a general anesthetic agent. They expressed the opinion that if ethyl chlorid came to be employed as a general anesthetic agent in practical surgery, there would be a record of sudden deaths through cardiac failure, proportionately even more numerous than those occurring under chloroform.

The past seven years' experience proves this view to have been erroneous. A careful perusal of their paper, together with the results of the Glasgow Committee's experiments on rabbits, makes one disposed to think that a too concentrated vapor was employed in both cases, and that the alarming fall of blood-pressure might have been due in part to this strong vapor acting on the laryngeal filaments of the vagus. Quite apart from this, it is obvious that the application of a stifling vapor to a dog or rabbit would of necessity produce such a degree of fright as to interfere markedly with the heart's action, even to the extent of causing complete arrest in some cases.

In the human species, however, it has been found by Malherbe and Laval that the blood-pressure does fall to about two-thirds of its normal during anesthesia, although the frequency of the pulse remains the same, but on return of consciousness the original pressure is at once regained.

Ruegg, of Basle, has arrived at results differing widely from those of Wood and Cerna, and in some degree from those of Malherbe and Laval. This observer finds that, while concentrated vapors of ethyl chlorid are found to produce death by respiratory spasm leading to asphyxia, normal vapors such as are commonly used for general anesthetic purposes stimulate both heart and respiration of the animals experimented on.

Cole, of Cambridge, states that the blood-pressure is not

affected to any great extent by small doses, but if any change does occur it is increased. With large doses the pressure is raised and remains high for a considerable time, but eventually it falls if the vagi are intact. If the vagi be cut no rise occurs, but a gradual fall is perceptible. The rise which occurs, of course, in this case is due to acceleration of the cardiac pulsations owing to cessation of the inhibitory vagal impulses.

The drug when given in small doses such as are used for ordinary anesthetic purposes has a marked stimulating effect on the respiration, the diaphragm being especially affected through its cerebral center. With large doses the stimulation becomes excessive and the diaphragm is brought into a condition of powerful tonic contraction, the heart continuing to beat strongly until death ensues.

With all but very large and excessive doses it is extremely easy to restore animation by means of artificial respiration, probably owing to the fact that the heart's action is so little impaired that, after even a prolonged inhalation of the drug, the medullary centers have not been rendered anemic.

The practical point to be deduced from this is that the chief danger with ethyl chlorid is paralysis of the respiration. It is essential for safety, therefore, that throughout an administration the most careful attention be paid to the breathing of the patient.

Rolland, of Bordeaux, has carefully investigated the action of ethyl chlorid (in the form of "Somnoforme") on the higher nerve-centers in men and in animals. He assumed that there must be microscopic evidence in a nerve-cell of the change wrought in it during anesthesia. This belief was so far based on the fact that other observers had noted such changes after large doses of alcohol. Binz described granular transformations in cerebral and cerebellar cells in animals which had been put under the influence of chloroform and morphin, such changes being apparent up to 24 hours after the administration of the chloroform.

Dr. Rolland's mode of investigation was as follows: An animal having been narcotized with somnoforme, a quantity of filtered solution of methylene blue, 3 per cent. in normal saline solution, was injected into the external carotid artery by means of a syringe. After a period of anesthesia varying from 5 minutes to an hour or more, the animal was killed and the brain examined. At the time control observations were carried out on animals of the same

type which had not been anesthetized and others which had been kept under the influence of somnoforme for an hour and then allowed to regain consciousness before being killed. In the animals which inhaled the drug and were killed during the anesthesia Rolland found the neurons modified in varying degree, according to the duration of the inhalation, and the region to which the cell belonged. The cells of Purkinje were modified in shape and volume and structure, as also were the pyramidal cells, the former being earlier affected, the latter only showing changes after the animal had been saturated with the anesthetic. Rolland described "moniliform," varicose, and irregular knotty conditions in the filiform prolongations of the cells. He employed the staining methods of Golgi and Nissl.

His conclusion was that ethyl chlorid or somnoforme acts on the cells of Purkinje, suppressing sensibility to pain, and that when saturation with the anesthetic is attained the pyramidal cells become affected, the sense of touch is suppressed, and loss of consciousness induced. He considers that the drug has "an elective action" on the cells mentioned, just as muscarin is known to have an effect on the ganglia of the heart and strychnin on the cellular elements of the spinal cord.

There seems to be room for considerable doubt as to whether Rolland is justified in coming to such definite conclusions as a result of his observations and experiments, when we bear in mind the fact that the functions of the cells of Purkinje and of the pyramidal cells are still in the domain of obscurity.

The muscular system is affected by "athetotic" movements when an animal is deeply under the influence of ethyl chlorid, the upper extremities being most affected, and this is due to central effects in brain and cord—the movements ceasing immediately on section of the motor nerves to the part.

The stomach and digestion are not directly affected by the inhalation of the drug, but the medullary centers are stimulated just like the centers for respiration. The occurrence of nausea and vomiting in certain cases is due to this. In prolonged cases of ethyl chlorid anesthesia vomiting may be due to direct irritation of the stomach, as after ether anesthesia, owing to the patient having swallowed mucus impregnated with ethyl chlorid.

The liver is not markedly affected in any way, but cases of

jaundice have been noted as a sequel to ethyl chlorid anesthesia, pointing to a disturbance of this organ.

Schifone finds that a short inhalation of 10 to 15 minutes has no effect on the character of the urine secreted, but that prolonged narcoses of an hour's duration or more aggravates any albuminuria which previously existed, and leads to albuminuria in some cases in which the urine has been previously normal in character.

Malherbe states that repeated doses of the drug on several days in succession cause fatty degeneration of the kidneys and liver, which tends to increase after the cessation of the administrations.

THE APPARATUS FOR ADMINISTERING ETHYL CHLORID

Various methods have been suggested for administering ethyl chlorid, but one can have no hesitation in saying that the closed method with a bag inhaler is the only reliable and satisfactory one. At the same time, for rendering a patient merely semi-anesthetized in order to go on with ether or chloroform anesthesia, a lint mask or a handkerchief folded into the form of a cone will often answer the purpose. When full ethyl chlorid anesthesia is required, however, for extracting a few teeth, or opening an abscess, failures are very apt to occur with this method. Breuer's mask, which might be described as a semi-open method, need only be mentioned to be condemned; and it was due to the use of this inhaler very generally that ethyl chlorid for some time made such slow progress and was considered uncertain in its action.

As regards the closed method, the essential parts of the inhaler are: (1) A good face piece with a pneumatic pad; (2) a rubber bag of about one gallon capacity; and (3) a metal angle junction with an aperture for spraying ethyl chlorid through, or a two-way stopcock.

In place of the two-way stopcock it is often convenient to have a small test-tube holding about 6 c.c. of ethyl chlorid attached to the lowest extremity of the bag by means of a rubber tube opening into the bag. This test-tube should be graduated or marked at 3 and 5 c.c., and by means of it a definite quantity of the drug can be administered as an initial dose, while if more be required it can be added subsequently through the aperture in the angle tube.

The rubber of the face piece and bag may be of the red or black

variety, but, on the whole, red rubber is the less acted on of the two by the ethyl chlorid. No part of the inhaler should be made of vulcanite, as this substance is soon made soft and friable by the action of ethyl chlorid.

As I have pointed out elsewhere, the essential parts of an ethyl chlorid inhaler exist in Clover's inhaler from which the ether chamber has been removed. At any rate, only the very slightest alterations are required, and these can be carried out by any instrument maker at a trifling cost. This is a point of some importance, as many country practitioners already possess a Clover inhaler, and thus no additional outlay is required. McCardie and Harvey Hilliard have advocated the use of an Ormsby inhaler for administering ethyl chlorid, and I can say from personal experience that it answers quite well, though I prefer to use the form of inhaler just described, as being a more exact method, and because the inhaler and the bag are more easily cleansed than the Ormsby apparatus.

The construction and advocacy of special inhalers for administering this anesthetic is to be deprecated. They are quite unnecessary, and are likely to lead to confusion and bad results. They are christened "Ideal," "Simplex," "Eureka," and are more calculated to further the interests of the pushing instrument maker than help the doctor or his patients.

I should also like to protest against the employment of lint in any closed inhaler for ethyl chlorid. This has been repeatedly recommended and referred to by writers on the subject—Mr. Jocelyn Swan, Dr. Penderville, and others. Not only is lint of no possible use in this connection, but it is a positive disadvantage. The method of using it generally described consists in placing inside the face piece a piece of lint cut specially to the shape of the face piece, and, having inserted a wire spring to retain it in position, to spray the ethyl chlorid over the woolly surface. My experience has been that the lint almost invariably freezes in places, whence the production of anesthesia is slower, while at the very start the vapor presented to the patient is far too pungent to be pleasant. Much ethyl chlorid is wasted owing to the freezing. This method has been employed largely with the view that ethyl chlorid has a destructive action on the rubber of the bag when sprayed directly into it, but I have not found this to be the case in the least

degree, and I now have in use in perfect condition bags which have been working for upward of two years.

PREPARATION OF THE PATIENT

The patient should have abstained from food for a period of not less than two hours prior to the administration of the anesthetic. If the stomach, rectum, or bladder be not nearly or quite empty beforehand, they are very likely to empty themselves reflexly, either during or immediately after the anesthesia, and this is particularly the case in children. If any dentures be present in the mouth they should be removed, and inquiries should be invariably made as to their presence. Anything tight about the neck or waist should be relaxed and the clothing generally loosened or removed.

POSITION OF THE PATIENT

As regards the anesthetic, there is no contraindication whatever to the use of the sitting position in the dental chair, or otherwise, but the surgeon may prefer to have the patient lying down for his personal convenience; this position is also more suitable for certain patients, such as young children. These patients are generally apt to slip down in the chair and collapse in a heap on the seat or the floor, to the annoyance and inconvenience of all concerned.

When the sitting position is used in adults care should be taken that the head be not put too far back, since if this be done the trachea becomes constricted by the neck muscles and the respiration becomes embarrassed. The coronal plane of the head should be in the same vertical axis as the spinal column.

THE ADMINISTRATION

Five c.c. of the drug is sprayed into the bag of the inhaler through the hole in the angle junction tube or decanted into the test-tube which has been described above. The face piece is then carefully adapted to the patient's face, and the patient instructed to breathe away quietly to and from the bag. If the ethyl chlorid has been placed in the test-tube, this should be taken between the thumb and forefinger and gradually raised along with the lower end of the bag. This must be done slowly, and not suddenly, as

otherwise the vapor will be too pungent and cause the patient to hold his breath.

After about six or eight full breaths the patient will commence to take deeper inspirations, and the pupils will contract somewhat, but will then almost at once begin to dilate and rapidly become dilated to a diameter of about 5 mm. and lose their reaction to light. Reboul says that the pupil is dilated in 40 per cent., contracted in 8 per cent., and unchanged in 52 per cent. of the cases.

The muscles become generally relaxed throughout the body, with the exception of the masseter muscles, which very often go into spasm.

This is one of the drawbacks to ethyl chlorid, and to avoid waste of time in opening the mouth the use of a mouth prop, inserted prior to commencing the inhalation, is desirable, as when using nitrous oxid gas. The patient's face flushes and sometimes beads of perspiration appear. The pulse is full and bounding, a sphygmographic tracing showing a clearly defined tidal wave.

The patient becomes unconscious in from 18 to 25 seconds, and on the average full anesthesia is obtained in 50.9 seconds, allowing an available period for operating of 71.3 seconds (McCardie).

The author has found, however, that whenever a longer period is desired it can be obtained, and with safety, in the vast majority of cases by pushing the administration, the longest period obtained in his experience being 5 minutes from the removal of the inhaler, the dose employed being 7 c.c. This was rather an exceptional case, however.

Drs. Malherbe and Laval, of Paris, have described three distinct stages in the anesthesia: (1) An analgesic stage, which commences after two or three breaths, and lasts for from 20 to 30 seconds; (2) an anesthetic stage, which they say lasts for 2 to 3 minutes; and (3) a second analgesic stage, during which the patient may move and talk but feels no pain.

AFTER EFFECTS

These vary considerably, but under ordinary circumstances cannot be considered serious. Some headache or dizziness, with nausea or actual vomiting, are the most common.

After pure ethyl chlorid I find from 20 per cent. to 25 per cent. of patients are nauseated to a greater or less degree, but the char-

acter of the nausea and vomiting is similar to that which we see after ether and does not last long. It is often over and done with in 10 to 15 minutes, and anything lasting longer than 3 or 4 hours is extremely rare. McCardie records a patient nauseated for 30 hours. Vomiting is much less common when nitrous oxid is combined with the drug, and then does not occur in more than 5 per cent. to 10 per cent. of the cases.

Much depends on the patient, of course, and the amount of preparation which he has undergone. If the administration has been undertaken unwittingly, immediately after a full meal, vomiting may be looked for, and, indeed, is almost certain to occur. I find that private patients are more likely to vomit than hospital patients, but Harvey Hilliard finds the contrary to be the case.

In cases in which the anesthesia was kept up for half an hour or upward by means of this anesthetic alone, violent and painful retching has often resulted. For this reason it is best not to maintain anesthesia with ethyl chlorid for longer than about 10 minutes.

Fainting and collapse are occasionally seen, but are usually associated with vomiting and nausea. Jaundice is uncommon, but some cases have been reported from Paris. Albuminuria is unknown except after prolonged narcoses of half an hour or more (Schifone). Fatty degeneration of the kidneys and liver has been noted after repeated administrations.

The drug has a distinct tendency to promote erotic thoughts and dreams, and even sensuous movements of patients while in the semi-anesthetic state. Subsequent accusations, made by females of indecent assault, etc., have been recorded. Marshall, of Liverpool, mentions two such cases. On regaining consciousness, hysteria with profuse shedding of tears is common in young girls.

ETHYL CHLORID IN GENERAL SURGERY

In almost every major operation requiring the eventual employment of chloroform or ether, it is best to induce anesthesia by means of ethyl chlorid, and then to pass on immediately to the chloroform or ether. In this way the struggling period is avoided, which, as Hewitt has pointed out, is the time when the large majority of chloroform fatalities occur. It is somewhat astonishing that at the present day in the United States as long as 15 minutes are required to anesthetize a patient, the reason being that ether is employed, and

is administered on the straw cuff, or an open cone. Apart from the waste of time, the patient is semi-conscious during a large portion of this time and striving to endure a most unpleasant, almost suffocating vapor. Hence it seems almost barbarous to subject a fellow-creature to this ordeal when with ethyl chlorid we can without any difficulty waft him into euthanasia in 25 seconds. The reason for such a long time being required to induce anesthesia is, we believe, due to the fact that Clover's portable inhaler has never met in the United States with the appreciation which it deserves, the open and semi-open methods of etherization being so generally used. It is, of course, necessary to use an inhaler on the same principle as the Clover if we wish to avail ourselves of the ethyl-chlorid-ether sequence.

It is in the minor operations of surgery, especially when carried out by the country practitioner unaided, that ethyl chlorid shows its greatest advantage. Indeed, I will go so far as to say that it is the only anesthetic (with the exception of nitrous oxid) which the medical man is justified in administering unless in exceptional circumstances without having a second medical man present to help him. The anesthetic is specifically suitable for such little procedures as opening superficial abscesses, tenotomies, passive movements of stiff joints, removal of external piles, application of the actual cautery, and removing dressings or a drainage tube from a wound.

ETHYL CHLORID IN GYNECOLOGY

While ethyl chlorid is no way adapted for midwifery practice, it is well suited to many gynecologic procedures. Ordinary vaginal examinations may be frequently carried out under ethyl chlorid anesthesia, although in cases in which complete abdominal relaxation is needed something more may be required. Curettage, dilatation of the cervical canal, and cauterization of a vascular caruncle are easily compassable under this anesthetic.

ETHYL CHLORID IN THROAT SURGERY

Ethyl chlorid undoubtedly has the strongest possible claims as the best anesthetic we possess for the more brief operations on the naso-pharynx and throat, such as the removal of adenoids, polyps, spurs on the septum, and tonsillotomy.

In some of these procedures it may be desirable or even necessary.
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sary to employ ethyl-chlorid-ether sequence in order to insure a sufficiency of time; in cases, for instance, in which adenoids are plentiful, requiring thorough attention, and tonsils also are present that have to be removed by means of guarded bistoury and volsellum, rather than guillotine, owing to their being flat and difficult to get hold of. But it may be safely said that a surgeon who is unable to deal with a simple case of adenoids or tonsils satisfactorily within the $1\frac{1}{2}$ to 2 minutes afforded by ethyl chlorid is not fit to operate on such patients at all.

It has been objected that in such cases the period occupied by these operations with ethyl chlorid as the anesthetic is unduly short, and in a private house the patient's friends may thus consider the operation actually more trivial than it really is or than is desirable for those concerned in its performance. But such an objection can scarcely be seriously advanced, for the skill of the surgeon is shown by the very rapidity with which the operation is completed. It also remains to be proved whether recurrences of adenoids are more common in cases which are dealt with under ethyl chlorid than when the less volatile and more slowly acting anesthetics are employed. In spite of its many advantages, the jaw spasm which is produced by ethyl chlorid is a drawback in adenoid operations, but this may be overcome by the insertion of a small wooden prop between the teeth prior to the commencement of the anesthetic, or when the anesthesia has been induced the teeth can be slightly separated by means of a small wooden mouth wedge and Doyen's gag inserted on the side opposite to that on which the surgeon stands.

The rapidity with which consciousness is regained with ethyl chlorid is a very great advantage in an operation associated with such free hemorrhage as is that of curetting the naso-pharynx. The patient recovers just in time to expel blood lying about the throat by his own voluntary effort, and if any blood, owing to insufficient sponging, has got dangerously near the rima glottidis or even past it, it is rapidly got rid of and no harm results.

Vomiting is rather more common than when ethyl chlorid is used for operations on the extremities, for instance, but this is due to blood being swallowed in many cases, and the vomiting of this blood which is a desideratum. It is brief in character, however, and the young patients are often clamoring for food long before anything more than boiled milk or beef tea is allowed them.

ETHYL CHLORID IN OPHTHALMIC SURGERY

It is not yet generally recognized by eye surgeons what a valuable general anesthetic is available for them in this drug. Camille Fromaget drew attention to its merits three years ago, and Sidney Stephenson has more recently confirmed his favorable opinion. Both consider it an almost ideal anesthetic from the ophthalmologist's point of view, and Stephenson had employed it on several hundred occasions. He finds it particularly useful in the out-patient department for purposes of diagnoses, especially when dealing with children. In cases of intense photophobia due to eczematous keratitis it acts admirably, and it is possible to induce anesthesia, examine the eye, and have the child conscious again inside five minutes—a point of great practical importance in hospital work. To carry out an ophthalmoscopic examination in refractory children, the child is placed in the nurse's arms in a convenient position as regards the lamp and the ethyl chlorid is administered.

The period of anesthesia is quite as long with a single dose of 4 to 5 c.c. as will allow of the examination of both fundi, and if need be of introducing a speculum, etc. Stephenson has carried out various minor operations on the eye by means of this anesthetic, such as passing a lachrymal probe, opening abscesses, extirpating Meibomian cysts, slitting the outer canthus, expressing the conjunctiva, tapping the aqueous humor, cauterizing corneal ulcers, paracentesis, needling the lens, and even dividing the recti muscles, and completely enucleating the eyeball.

ETHYL CHLORID IN DENTAL SURGERY

Probably in no field is ethyl chlorid destined to be of greater service than in dental surgery. Certainly up to the present it has been used to the greatest extent in this branch of surgery. Were it not for the masseteric spasm, so commonly seen when this drug is employed, there is almost no dental operation which could not be carried out successfully with ethyl chlorid as the anesthetic; but it is the experience of practically all those who have worked with the drug in dentistry that it is advantageous to combine it with nitrous oxid or ether in the large majority of cases.

Ether will be of most service when the extraction which it is desired to carry out is extensive, and a long anesthesia with a fully relaxed jaw is needed. But even in such cases much time is saved,

and a good deal of after-vomiting is avoided if the ether be preceded by ethyl chlorid. On the other hand, in short cases in which the anesthesia afforded by nitrous oxid alone is too brief, a mixture of 3 gallons of nitrous oxid with about 4 c.c. of ethyl chlorid will afford in most cases an anesthesia of upward of a minute and a half, while vomiting after such a case is almost as rare as after gas alone. I have found that not more than 5 per cent. of such patients are sick after the anesthetic, and this is absolutely confirmed by Mr. Guy, who has a very large experience in such cases, both in private practice and at the Dental Department of the Royal Infirmary, Edinburgh.

SOME CLINICAL CASES

CASE I.—Male, aged 39 years. Tall and powerfully built. Operation for removal of a fibroma of the forehead. Anesthesia induced in 80 seconds and lasted for 15 minutes. Ethyl chlorid required, 20 c.c. After four minutes the patient turned somewhat dusky owing to jaw spasms; the mouth was opened, and tongue traction exercised, causing relief of the spasm and a return to the normal. The patient was a little drowsy afterward, but had no vomiting. The spasm seen here was quite typical of what we have had to guard against in using ethyl chlorid continuously, and could probably have been avoided by administering a less amount of the drug.

CASE II.—Male, aged 40 years. Phlegmonous condition of the shoulder and arm. The patient was a strongly built laborer, suffering from lobar pneumonia at the time. His temperature was 102.7° F. Eight to 10 c.c. of ethyl chlorid was sprinkled on a handkerchief, which was at once held like a compress over the nose and mouth. Anesthesia was induced in less than a minute, and the parts incised and explored without the patient evincing any signs of pain. There were no after effects.

CASE III.—Male, aged 79 years. His heart was weak, and he suffered from pleural effusion. He was seated in a chair, and anesthesia induced with 5 c.c. of ethyl chlorid, and was continued for 8 minutes. The pleural cavity was tapped, and 70 ounces of fluid withdrawn. No vomiting or ill effect of any sort ensued.

CASE IV.—Female, aged 22 years. Seven teeth were extracted. Anesthesia was induced with ethyl chlorid in 45 seconds, and was

available 75 seconds. Amount of drug used was 7 c.c. No ill after effects.

CASE V.—Female, aged 14 years. Four teeth were extracted. Anesthesia was induced in 55 seconds, and was available 80 seconds. No ill after effects.

CASE VI.—Female, aged 19 years; thin and anemic. Twenty-five teeth were extracted. Anesthesia was induced in 65 seconds, and was available 5 minutes. Seven c.c. of ethyl chlorid was used. No ill after effects.

CASE VII.—Female, aged 40 years. One tooth was extracted. Deep anesthesia was induced with 6 c.c. of ethyl chlorid in 65 seconds, and lasted 2 minutes. Pupils were rather dilated and breathing was stertorous. The patient was very sick (nausea and vomiting) at once. Had been travelling for several hours by rail, and meals had been irregular.

CASE VIII.—Female, aged 36 years. Bimanual examination. Used 10 c.c. ethyl chlorid. Anesthesia was induced in 70 seconds, and lasted 2½ minutes. The muscles of the abdomen were completely relaxed. No vomiting or discomfort followed.

CASE IX.—Male, aged 17 years. Enucleation of an eye. The patient was anesthetized in 80 seconds, and anesthesia was available 2 minutes. Seven c.c. was used. The surgeon being a rapid operator, was able to remove the eye with ease in the time available.

CASE X.—Male, aged 5 years. Adenoids and tonsils. Five c.c. used. Induction of anesthesia in 40 seconds; continued 75 seconds. No vomiting.

CASE XI.—Female, aged 19 years. "Wen" on the scalp. Anesthesia was induced in 65 seconds, and maintained for 15 minutes. Fifteen c.c. of ethyl chlorid was used. No change of color or cyanosis. Good, quiet anesthesia, with slight stertor from the commencement. The patient awoke from the anesthetic sleep seeming quite bright, and after a slight attack of retching walked back to her bed.

CASE XII.—Male, aged 8 years. Circumcision. Twelve c.c. was administered. Induction of anesthesia in 65 seconds; duration, 15 minutes. On recovery there was slight retching of frothy mucus, but no other discomfort.

CASE XIII.—Female, aged 35 years. Sacro-iliac disease. This patient was in a very weak and exhausted condition and was scarcely

fit to take a general anesthetic. Ethyl chlorid was chosen, with the idea of maintaining a light degree of anesthesia, from which the patient might be allowed to recover rapidly if desirable. The patient was anesthetized in about 50 seconds and kept anesthetized 35 minutes, while the operation was completed. Her condition on regaining consciousness was wonderfully good, although there was a good deal of vomiting. Twenty-seven c.c. ethyl chlorid was used.

CASE XIV.—Male, aged 14 years. Fibrous ankylosis. Anesthesia was induced in 60 seconds and maintained for $1\frac{1}{2}$ minutes. The adhesions were broken down with ease. No ill after effects.

CASE XV.—Girl, aged 6 years. Operation for club-foot. Four c.c. ethyl chlorid was used in a bag inhaler (Hewitt's). Anesthesia was induced in 50 seconds, whereupon the chloroform-ether mixture was substituted. Anesthesia was maintained and operation commenced in 6 minutes, and concluded in 10 minutes. There was no struggling or resistance at any period. Slight athetotic movements. No vomiting.

CASE XVI.—Female, aged 40 years. Operation for extraction of 20 teeth and stumps. Five c.c. ethyl chlorid used for 30 seconds, when ether was rapidly switched on. Inhalation was continued for $3\frac{1}{2}$ minutes, when the inhaler was removed and extraction begun. This occupied 12 minutes exactly, but the patient required no second application of the inhaler, nor did she make any movement from start to finish. Careful sponging was carried out. The patient was left lying comfortably, having shown no symptom of sickness.

CASE XVII.—Female, aged 38 years. Two difficult teeth to extract. Anesthesia was induced with 5 c.c. of ethyl chlorid, and continued with ether, which was administered for 3 minutes. The inhaler was then removed and an available period of 4 minutes obtained for the operation, which was completed with ease in the time. The patient was not in the least sick, but complained of her lip being hurt with the gag.

FATALITIES RECORDED

Under Somnoforme.—(1) At Enfield, in March, 1904, a stout, healthy woman, 40 years of age, who had never had any serious illness, but had fainted on one occasion, was to be anesthetized for a dental operation. Ether was suggested as the anesthetic, but was refused, and somnoforme was decided on. Anesthesia was induced

and seven teeth extracted, when the breathing suddenly became shallow and stopped. The medical man and two dentists who were present used all the ordinary restorative measures, but without avail. The amount of somnoforme used was not recorded.

(2) At Llandudno, 1904. The patient, a female of spare build, was aged 42 years. The operation was a dental one. Gas had been taken previously without any difficulty. Anesthesia was induced with 2.5 c.c. of somnoforme, but before the operation was begun the patient became very pale and the breathing shallow, eventually stopping altogether. Restorative measures were of no avail. No inquest was held.

(3) Another fatal case occurred at Swansea in 1904, but details have not been available.

Under Ethyl Chlorid.—(1) The following case occurred in v. Hacker's clinic in the hands of Lotheissen, who records the case. On October 23, 1899, a laborer was narcotized with ethyl chlorid ("kelene") in order that a skin-grafting operation might be carried out. He had been under the influence of the drug for about 3 minutes when the blood was noticed to be markedly darker in color. The patient, who was a heavy drinker, had a moment before shown violent excitement and fresh kelene had been sprinkled on the mask. When facial cyanosis was noticed, however, the mask was removed and corneal and pupil reflexes were found to be absent. Then violent twitchings were observable in the limbs, while intense trismus was present. The pulse, though not countable by reason of the violent muscular spasm, was distinctly palpable, although the patient only breathed spasmodically. All at once it stopped, and all attempts at restoring it were in vain. About 10 c.c. of the drug was used. Marked eccentric hypertrophy of the heart was noticed, with sclerosis of both the aorta and coronary vessels.

(2) Bossart records the following case: The patient, a child aged $1\frac{3}{4}$ years, suffered from laryngeal diphtheria. Three c.c. ethyl chlorid was administered on a compress in order to perform a tracheotomy. Suddenly during the tracheal incision breathing stopped, cyanosis appeared, and the pupils became widely dilated, while the pulse became imperceptible. The child died. At the autopsy an enlarged thymus gland and diphtheritic membrane below the false vocal cords were found. Death was due to cardiac failure, caused by diphtheritic toxin or by ethyl chlorid.

(3) Olcott Allen records the following: A colored man, aged 28 years, an epileptic, was being operated on for strangulated hernia. Anesthesia was started with ethyl chlorid, and a change to ether was made when 15 c.c. had been used. Just as the ether was started the patient vomited an enormous quantity of almost clear watery fluid, which spouted from his mouth in a continuous stream without any retching or respiratory effort. This could not be controlled, and lasted for about 3 minutes. When it stopped at last the respiration had also ceased and cyanosis was present. The pulse had stopped. Artificial respiration with tongue traction was carried out, but without any effect. No air seemed to enter or leave the chest. No tracheotomy was done, and the friends refused an autopsy.

(4) Ware has recorded another *bona fide* case of death under ethyl chlorid narcosis—out of 12,436 cases which he collected.

(5) McCardie, Seitz, of Zurich, and Th. Kocher, have also placed on record cases in which death took place at periods varying from an hour to a week after the narcosis, but they can scarcely be seriously attributed to the effect of ethyl chlorid.

At Stourbridge (Worcestershire), a stout, alcoholic female, aged 50 years, was given 6 c.c. of ethyl chlorid in order that a minor operation on her finger might be carried out. She was just regaining consciousness when the pulse and breathing suddenly stopped, and restorative measures were futile. The cause of death was probably syncope. The necropsy revealed a dilated stomach, fatty liver, and cirrhotic kidneys. The heart was empty.

(6) A man, aged 28 years, approximately, died in a hospital in Edinburgh in July, 1905, from ethyl chlorid. Details are lacking.

(7) A female, aged 50 years, died under ethyl chlorid in Edinburgh on July 26, 1905, in a dentist's hands. The patient had a feeble heart, and had recently had two attacks of pneumonia. Her medical man had warned her of the danger she would run by taking an anesthetic, but she went unknown to him and arranged with a dentist to give her ethyl chlorid. Death was instantaneous.

(8) A death under ethyl chlorid occurred at Plymouth (England), in July, 1905. Details are lacking.

Numerous cases have been recorded in which asphyxia, due to obvious overdose, occurred, but was relieved at once by artificial respiration. Gargam records several of these, and Bossart one in which 30 c.c. were placed in the inhaler without any worse result

than easily relieved asphyxial symptoms. From the cases noted above, then, we have two deaths in practically healthy patients for trifling operation under somnoforme, and eight deaths under ethyl chlorid, from which, at any rate, we can eliminate Bossart's as being obviously due to causes other than the anesthetic. Seitz has collected a series of cases numbering 17,000, with only one fatality (Lotheissen's case), and Ware, working in a comparatively different area, arrives at almost the same results.

BIBLIOGRAPHY

- Adam, J., Ethyl Chloride as a General Anesthetic, *Glasgow Med. Jour.*, 1902, ii. 260.
- Alker and Lafite-Dupont, Le chlorure d'ethyl comme Anesthesique generale, *Gaz. hebdomadaire de Bordeaux*, 1903, xxiv, 29.
- Allen, Olcott, Death during Ethyl-Chloride Anesthesia, *Amer. Jour. Med. Sci.*, December, 1903.
- Billeter, Aethyl-chlorid zur totalen Narkose, *Schweizer Vierteljahrschrift für Zahnheilkunde*, 1898, viii.
- Blank, Aethyl-chlorid Narkose, *Deutsch. Zahnärztl. Woch.*, 1901, No. 8.
- Blumfield, J., Recent Work in the Field of General Anesthetics, *Practitioner*, 1903, lxxi, 420.
- Bossart, A., Aethyl-chlorid Narkose, *Correspondenzblatt für Schweizer Aerzte*, xxxii, No. 19.
- Boyle, H. E. G., Somnoforme Anesthesia, *St. Barthol. Hospital Jour.*, xi, 51.
- Braine, Carter, Anesthetics in Dental Surgery, *Brit. Dent. Jour.*, 1904, ii, 717.
- Brodthsch, A., Suggestirte Narkose vermittelt Ethylchlorid, *Schweizer Vierteljahrschrift für Zahnheilkunde*, 1898, viii.
- Bryan, W. J., Ethyl-Chloride as a General Anesthetic, *Amer. Practitioner*, August, 1903.
- Buxton, Dudley, Anesthesia in Operations on the Upper Air-Passages, *Practitioner*, 1905, i, 77.
- Carlson, *Zahnärztl. Wochenblatt*, Hamburg, June, 1895.
- Chaput, *Münch. med. Woch.*, 1902, 1245.
- Clover, J. T., On Dichloride of Ethidene as an Anesthetic, *Brit. Med. Jour.*, 1880, i, 797.
- Cole, Sidney, The Physiological Action of Ethyl Bromide and Somnoforme, *Brit. Med. Jour.*, i, 1421.
- Dalban, L., Les differents modes d'emploi du chlorure d'ethyle en chirurgie dentaire, *L'Odontologie*, xxxiii, 85.
- Daniell, G. W. B., Ethyl-Chloride Apparatus and a New Method of Administration, *Lancet*, 1903, ii, 1087; The Administration of Ethyl Chloride, *Brit. Med. Jour.*, 1904, i, 949.
- Doyen, *Revue critique de Médecin*, March, 1901.
- Dumont, Aethyl Chlorid: Ueber den gegenwärtigen Stand der allgemeinen Anästhesie (a pamphlet), 1901; *Handbuch der Anästhesie für Aerzte*, 2te Aufl., 1904.

- Eastham, T., Narcotile Anesthesia, *Lancet*, 1903, i, 1091.
- Fleming, A. L., Ethyl Chloride; a Few Practical Remarks, *Brist. Med.-Chirurg. Jour.*, September, 1904.
- Gurard, H., Le chlorure d'éthyl en anæsthesie generale, *Revue de Chirurgie*, **xxii**, 704 and 883.
- Guy, W., The Administration of Ethyl Chloride or Somnoforme, with a Description of a New Inhaler, *Jour. Brit. Dent. Ass.*, 1904, 249; A New Inhaler for Gas, Ether, or Ethyl Chloride, alone, in Mixture, or Sequence, *Jour. Brit. Dent. Ass.*, 1905, 606; Aethyl Chlorid, *Münch. med. Woch.*, 1902, 1942.
- Haslebach, Experimentale Beobachtung über die Nachwirkung der chlor-ethyl Narkose, Inaugural Dissertation, Berne Medical Congress, 1901.
- Hatch, R. M., Ethyl Chloride as a General Anesthetic, *Brit. Dent. Jour.*, 1903, i, 638.
- Hedsted, Universal klorethyl Narkose, *Hosp. Tid.*, ix, 1010.
- Hewitt, F. W., Anesthetic Effects of Ethyl Chloride, *Lancet*, 1904, ii, 1408 and 1486; A New Method of Anesthetization for Dental Practice, *Brit. Dent. Jour.*, 1903, 615.
- Hilliard, Harvey, Ethyl-Chloride Narcosis, *Practitioner*, 1905.
- Kelly, Ethyl Chloride, *St. Mary's Hospital Gazette*, November, 1903.
- Kingsford, Ethyl Chloride Inhaler, *Lancet*, 1904, iii, 1639.
- Kitchen, E. H., A Simple Method of Administering Ethyl Chloride, *Brit. Med. Jour.*, ii, 1638.
- Kocher, Th., Operative Surgery, 2d English ed., article "Anesthesia."
- Koenig, Ueber ethyl-chlorid Narkose, Inaugural Dissertation, Berne, 1900.
- Lebet, Sur les effets physiologiques de Chlorure d'éthyl, *Thèse Inaugurale*, Berne, 1902.
- Le Dentu, Narkose mit Ethyl Chlorid, *Münch. med. Woch.*, 1902.
- Levy, A., The Administration of Chloride of Ethyl, *Brit. Med. Jour.*, 1904, i, 420.
- Llewellyn, T. L., Apparatus for Ethyl Chloride, alone or with Ether, *Lancet*, 1904, ii.
- Lotheissen, Zur Statistik der ethyl-chlorid Narkose, *Centralblatt für Chirurgie*, 1903, **xxx**, 522. Ueber die Gefahren der ethyl-chlorid Narkose, *Münch. med. Woch.*, May, 1900, 601.
- Ludwig, Ueber Narkose mit Ethyl Chlorid, *Beiträge für klinische Chirurgie von Bruns*, 1899, lvii.
- Luke, T. D., Anesthesia for Throat Operations, *Edin. Med. Jour.*, July, 1904, iii, 29; Anesthesia in Dental Surgery, chapter on "Ethyl Chloride," *Rebman Company, Ltd.*, 1903; Present Position of Ethyl Chloride as a General Anesthetic, *Lancet*, 1903, ii; Note on Ethyl Chloride, *Brit. Med. Jour.*, 1903, i; The Use of Ethyl Chloride as a General Anesthetic, *Edin. Med. Jour.*, 1903, ii, 425; Guide to Anesthetics, chapter on "Ethyl Chloride," published by Wm. Green & Son., *Edin.*, 1905, 2d ed.; New Inhaler for Ethyl Chloride, *Lancet*, July, 1903, ii.
- McCardie, W. J., A Few Cases of Ethyl-Chloride Narcosis, *Lancet*, 1900, i, 698; Inhaler for Ethyl Chloride, *Lancet*, 1901, i, 481; Some Further Cases of Ethyl-Chloride Narcosis, *Lancet*, ii, 123; Ethyl Chloride as a General Anesthetic, *Lancet*, 1903, i, 954; Some Remarks on Anesthetics in Dental Surgery, *Brit. Dent. Jour.*, 1902, 249.

- Mackie, J., Ethyl Chloride as a General Anesthetic in Nasal Surgery, *Brit. Med. Jour.*, ii, 895.
- Malherbe, Success of Ethyl Chloride as a General Anesthetic, *Münch. med. Woch.*, 1901, 1858; *Bulletin de Laryngologie*, 1902.
- Malherbe and Roubinovitch, Allgemeine Narkose mit Chlorethyl, *Münch. med. Woch.*, 1902, 1319.
- Matthess, Aethyl Chlorid, *Prager med. Woch.*, 1899, No. 17; Ueber die Narkose mit Chlor- und Brom-Aethyl bei kleineren gynäkologischen Operationen, *Prager med. Woch.*, 1899, xxiv, No. 17.
- Moritz, Ethyl Chloride and Nitrous Oxide Gas, *Lancet*, 1903, ii, 1368.
- Nieriker, Aethyl-chlorid Narkose, *Münch. med. Woch.*, 1902.
- Nogue, Sur l'anaesthesie generale par chlorure d'ethyl pur, *Archiv. de Stomatologie*, September, 1902.
- Nove Josseland, Sur le chlorure d'ethyl comme anaesthesique général, *Lyon. Med. Cli.*, 1903, 48.
- Poritt, N., Ethyl Chloride Anesthesia, *Brit. Med. Jour.*, 1904, ii.
- Prenderville, A. de, Ethyl Chloride in Surgical and Dental Practice, 1903 (a pamphlet); The Advantages of Ethyl-Chloride Anesthesia, *Lancet*, 1904, ii, 978.
- Reboule, Anaesthesia générale au chlorure d'ethyl, *l'Odontologie*, xxxiii, 39.
- Richardson, B. W., Articles in the *Asclepiad*, ii, 257, iv, 135; *Medical Times and Gazette*, December, 1867, 693; *ibid.*, May and June, 1868.
- Rolland, Influence of General Anesthesia on Nerve Centres, *Brit. Dent. Jour.*, 1903, 650.
- Schifone, La narcosi di cloro etilico, *Il policlinico*, June, 1904, xi, 258.
- Seitz, Deutsche Monatschrift für Zahnheilkunde, January, 1899, i; Schweizer Vierteljahrschrift für Zahnheilkunde, 1899; Zahnärztliche Rundschau, October, 1899; Deutsche Zahnärztl. Woch., Nos. 68 and 84, 1899; *Münch. med. Woch.*, 1901, 354.
- Stephenson, S., Ethyl Chloride in Ophthalmology, *The Ophthalmoscope*, 1904, 129.
- Syme, W. S., Ethyl Chloride as a General Anesthetic, *Lancet*, 1904, ii, 997; Ethyl Chloride as a General Anesthetic in Short Operations on the Throat and Nose, *Glas. Med. Jour.*, 1904, 215.
- Thiesing, Ueber Ethyl Chlorid, *Deutsche Monatsch. für Zahnheilk.*, April, 1896.
- Tottle, Experience with Kelene as a General Anesthetic, *Trans. N. Y. Med. Assoc.*, 1903.
- Wade and Finniemore, Ethyl Chloride in Chloroform, *Jour. of the Chem. Soc.*, 1904, 938.
- Ware, Martin W., The Field for Ethyl-Chloride Narcosis, *N. Y. Medical Record*, April, 1901.
- Wiessener, Ueber Ethyl-Chlorid Narkose, *Wien. med. Woch.*, 1899, xxviii, 1333.
- Williams, Ethyl-Chloride Inhaler, *Lancet*, 1904, i, 163.
- Wood and Cerna, The Physiology of Ethyl Chloride, etc., *Dental Cosmos*, July, 1892.
- Wood, J. M., Ethyl-Chloride Inhaler, *Lancet*, 1904, i, 1733.

THE DIFFERENTIAL DIAGNOSIS OF TUMORS OF THE RIGHT HYPOCHONDRIUM

A CLINICAL LECTURE

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GENTLEMEN: The unusual number of cases of kidney disease now in our wards affords me an opportunity of speaking to you about the difficulties you may encounter in examining tumors of the right subcostal region.

Here is a patient who entered the hospital November 9, 1904, complaining of severe pain in the right hypochondrium and of swelling of that region, the affair having followed an acute course. Symptoms began three days previously. Suddenly, in perfect health, without warning or previous attack, she was seized, on awakening, with very violent pain in the epigastric region, which pain soon extended to the entire right side. It was followed by bilious vomiting, the abdomen became distended, and all motions and passage of flatus ceased. A purgative prescribed by her physician produced a slight evacuation; but the symptoms did not improve; the pain remained as severe as ever, whereupon the patient decided to go to the hospital.

On examination, we found the abdomen tense and distended; palpation detected diffuse tumefaction, without precise limits, including the whole right side from the iliac fossa up to the false ribs. This examination caused acute suffering, the maximum intensity of which was at equal distance from the umbilicus and the upper and anterior iliac spina, that is to say, at MacBurney's point. The swelling was fixed, and did not follow the movements of breathing. Percussion showed that there was dulness over the region, and that this dulness rose as high as the false ribs, where it could not be distinguished from the liver dulness; below it descended as far as the lower third of the iliac fossa.

The general symptoms were not very marked; temperature was

normal, whereas the pulse was rapid, 120, but strong, an instance of the condition we know as dissociation. Her appearance was good, the urine contained neither sugar, albumin, nor biliary pigments, and there was no icterus.

In presence of this clinical situation, the first diagnosis that occurred to the mind was that of appendicitis, with circumscribed peritonitis having occasioned a large area of thickening about the colon. It is true, this thickening reached higher up than is usual, but this could be accounted for by a retrocecal, almost subhepatic form of appendicitis, due to an abnormal position of that organ; this was, indeed, the diagnosis that had been made before I saw the patient. The treatment usually applied to such cases was prescribed: water diet and applications of ice.

When, however, the patient was more closely examined, it was found that the bottom of the iliac fossa was accessible, and the palpation made it possible to pass from the crural arcade as far as the upper strait of the pelvis; the sensation thus acquired was that, though the tumor occupied the iliac fossa, it was not at home there, but came from further above. If, in the same way, its sensitiveness was examined, a painful maximum was unquestionably to be found at the classical point for appendicitis, but another maximum also existed beneath the false ribs and at the outer edge of the rectus muscle, which is the elective spot for gall-bladder pain. Again, the dulness referred to could not be distinguished above from that of the liver, a very unusual occurrence in peri-appendicular suppuration, where there is generally a strip of resonance beneath the liver. For these three reasons—finally and particularly because I found that the seat of pain increased steadily as the gall-bladder was approached—I set aside the diagnosis of appendicitis, and made that of pericholecystitis, probably of calculous origin.

During the days that followed the physical signs that I have just enumerated changed rapidly. The swelling almost melted away before our eyes, and disappeared in a characteristic manner, losing all connection with the iliac fossa, and acquiring a clear boundary at the bottom, whereas its relations with the liver remained and grew more marked. Mobility also appeared, and by the fourth day the tumor slightly followed the movements of breathing. Pain disappeared almost entirely; there remained no more than an uncertain sensitiveness of the entire region. MacBurney's point was still a

little sensitive; but the maximum of sensation was higher up, immediately below the edge of the ribs, at the gall-bladder point. It was evident that the liver and not the appendix was the organ involved. Freed from the inflammatory mass that connected it with the omentum and intestine, the gall-bladder could be made out enlarged. Motions were normal; urine contained no biliary pigments, and there were no signs of cholemia. Cross-questioned again as to her past liver history, the patient remembered to have had a hepatic colic several years previously. We were, therefore, certainly in presence of cholelithiasis with non-suppurative acute pericholecystitis, since there had been neither rigor nor pyrexia, and without obstruction of the excretory bile ducts, since there was no icterus.

The operation, performed November 17, confirmed the diagnosis fully. We found the gall-bladder distended and adherent to the colon and omentum; at its base was a green patch of gangrene that did not bleed on section, and beneath which could be perceived the angle of a calculus which was, so to speak, putting its head out of the window. We extracted about a dozen calculi, drained the wound, and the patient recovered.

I have related this case because it shows how many difficulties may arise in the diagnosis of these tumors of the right hypochondrium. In this instance the trouble at the outset was to distinguish between appendicitis and cholecystitis, and you saw how a careful study of the painful points was of the utmost importance in unravelling the order in which the accidents had occurred. In some cases the diagnosis is complicated by the possibility of the symptoms having a renal origin. Kidney, liver and gall-bladder, and colon and appendix are the three groups of organs that must be interrogated in the presence of a tumor of this region.

To begin with, you must search for the exact seat of the pain. The patient will often himself point it out with great precision; in other cases, as in the present one, the pain is diffuse, and only by perseverance will you succeed in definitely localizing its culminating point.

Appendicular pain corresponds to what is called MacBurney's point. Its value has been much discussed; and, although it should not be overrated and be considered as a pathognomonic sign, we may say that in the great majority of cases this point corresponds to the projection of the appendix on the abdominal wall. Taken with the

other signs of appendicular trouble, it affords strong presumptions in favor of that complaint. But we should not forget that the pain of appendicitis may descend toward the pelvis until it cannot be distinguished from the ovarian center of pain; and that again, when the appendix is subcecal, or when its inflammation is complicated with a certain degree of typho-colitis, the pain may rise along the line of the large intestine and approach the edge of the ribs.

In opposition to the appendicular center we find the cystic center which arises in cholecystitis and pericholecystitis. The gall-bladder projects itself on the abdomen at a point situated at the intersection of the outer edge of the rectus muscle and of the tenth rib; it is there that you find the painful maximum in biliary lithiasis.

Quite frequently it is propagated toward the epigastrium, constituting in this way the epigastric center; ascending radiations (the scapular center) are also observed in the right shoulder, breast, and mammary region. The pain seems even sometimes to follow the phrenic nerve and to reach the right side of the neck, the nape of the neck, and occasionally the head. Descending radiations are less frequent.

Between these two seats of pain we have the renal pain. It will be found below and farther out than the gall-bladder center, above the appendicular point, at a spot situated farther out than the external edge of the rectus muscle, at the level of the umbilicus. But this anterior painful localization is of less value than its posterior localization. Behind, it takes in the entire lumbar region; its radiations are mostly downward, and reach the scrotum or libia, and the inguinal canal; less commonly they occur in the direction of the thorax and upper limb. This renal pain sometimes gives rise to functional impotence of the entire side. I am constantly showing you examples of this in these wards that abound in renal diseases.

From the foregoing you will see that these three painful spots differ theoretically in their positions and radiations; but there are border cases in which we are quite unable to distinguish between them. You must then make your diagnosis from the physical character of the tumor.

Appendicitis generally gives rise to swelling in the badly defined limits, seated on the iliac fossa, motionless, and separated clearly from the hepatic dulness by the resonance of the large intestine.

These typical cases are easy to diagnose. But, according to the position of the appendix, forms can be observed whose diagnosis will present difficulties. We have already spoken of the subcecal variety, which gives rise to inflammation situated high up and extending toward the lower aspect of the liver, from which it cannot easily be separated. At other times you meet with movable tumors without connection with the wall and resembling floating kidney to a surprising degree. These are cases in which the periappendicular inflammation has simply agglutinated the neighboring coils without affecting the parietal peritoneum, a situation that is dangerous, since a perforation into the peritoneal cavity is always to be feared, and will not be guarded against by adhesions.

Tumors of the kidney are generally distinctly lumbo-abdominal: they fill more or less completely the fossa of that name, and produce in some instances deformity of that region; they have evident contours, a smooth surface, and a lower end easy to distinguish, whereas the upper disappears beneath the ribs; when taken between the two hands, one in front and the other behind, they can be tossed to and fro, and they slip back into the lumbar fossa; finally, they are separated from the anterior abdominal wall by the resonance of the ascending colon, resonance that is superficial, and must be looked for by means of gentle percussion. But in voluminous renal tumors, which come into direct contact with the anterior wall, the colon is thrown outward, and we are then deprived of this classical sign.

The type of renal tumor as just described is furnished by hydronephrosis, and particularly by intermittent hydronephrosis, which, in the periodicity of its painful crises, has the greatest resemblance to the clinical type described at the beginning of this lecture.

Suddenly, often without any cause whatever, without connection with the meals, the crisis comes on, with its acute suffering at the point described, its radiations, and characteristics; it is of such a kind that the patient remains motionless in an attitude of defence, bending forward or to one side. Alimentary or bilious vomiting, oliguria, or even complete anuria, make up the tableaux.

The disappearance of the crisis occurs quite suddenly, as did its beginning, sometimes after the kidney has been untwisted by the physician, and is almost always followed by temporary polyuria, as happens after nearly all painful visceral crises, but is more pronounced in these cases through the mechanical evacuation of the

hydronephrotic pouch. In the meantime the kidney resumes its primitive size and characteristic shape; the hydronephrosis has disappeared, and nothing remains but the floating kidney.

Other renal lesions may give rise to more or less periodical painful attacks. I have shown you such in renal lithiasis, tuberculosis, and even cancer. In this connection the history of a man still in our wards will be of interest.

He entered the hospital October 26, 1904, on account of pain situated in the hypochondrium. In his hereditary antedecents we find that his father died of pulmonary congestion, while his mother is tubercular; among his personal antecedents there are, on the other hand, repeated attacks of bronchitis, tenacious laryngitis, and possibly malaria brought from the colonies. His present illness began eight months ago, its first symptoms consisting in diffuse abdominal pain, predominating on the left side, and by great loss in weight. The patient then perceived in his side a tumor that varied in size at certain moments, while his urine would become temporarily purulent. There was never any pyrexia.

On entering the ward he was found to have a large mass occupying the entire hypochondrium, extending to the umbilicus, hard, dull, round at the lower end, slightly irregular, and rounded at the sides, not very movable, unaffected by breathing,—in a word, the character of a renal tumor. Pressure gave rise to pain, radiating toward the corresponding thigh. Urine was transparent, without sugar or albumin; the bladder, prostate, and testicles were normal. There were pleural rubbing sounds at the left base, and a few crackling rhonchi at the apex of the same side. The latter signs, as well as the patient's antecedents, decided me in favor of renal tuberculosis; and the operation, performed a few days later, showed that the diagnosis was correct.

All the varieties of renal tumors that we have passed in review were aseptic; but almost all can become infected and then give rise to the different forms of pyonephrosis. Let me recall to your memory a curious case that we saw here not long ago. An ill-defined lumbo-abdominal tumor, with uncertain anatomical origin,—kidney or colon; its inflammatory origin was certain, and yet there was no general reaction. Nothing but a blood-analysis, with 37,000 leukocytes, enabled us to be sure of suppuration. It turned out to be a perirenal abscess around a floating kidney, with its

fatty capsule suppurating in its abnormal position in the iliac fossa.

We must now pass on to hepatic or perihepatic tumors. Their essential characteristics are the continuity of their dulness with that of the liver, and their alternate rising and falling with the breathing movements.

A hydatid cyst of the lower aspect of the right lobe will present all of these characters; but in some instances, in which a frail pedicle attaches it to the liver, it may appear movable between the hands fore and aft, and have the other characters of a renal tumor. I showed you, as you may remember, an adenoma of an erratic lobe of the liver, which I removed under these conditions.

But it is particularly the tumors of the gall-bladder that give rise to mistakes, as we saw in the case of the patient that formed the subject of this lecture, and it is they that you will have to differentiate from periappendicular inflammation and certain renal tumors.

Biliary lithiasis occurs in the most varied forms. Pure hepatic colic is its prototype; but vesicular colic interests us most here. The cardinal signs are the same in both cases: sudden onset, acute pain at the cystic point, with radiations described above, vomiting, first alimentary and then bilious, thready pulse; pyrexia depends on the condition of asepsis or infection of the bile ducts. Icterus is lacking, which distinguishes this form from the full colic with migration of the calculus into the choledochus. These attacks of vesicular colic are longer, sometimes interrupted by periods of calm, and accompanied by very marked nervous reactions.

Locally, several varieties may occur. You may find diffuse swelling, almost impossible to outline, going perhaps clear down into the iliac fossa, hardly movable, and dull, as with our patient. But usually this swelling quickly decreases and shows a definite outline,—the edema of the omentum disappears, its connection with the colon ceases, and the tumor becomes evidently subhepatic and vesicular. You will then find it regular in shape, rounded, elastic, and sometimes fluctuating, and it will rise and fall with breathing; slight movements of laterality can be imparted to it.

Its size varies and sometimes changes from day to day, and the dulness naturally follows the same fluctuations; it is a tumor that may disappear, like intermittent hydronephrosis. In some instances

palpation enables calculi to be felt, and even a sort of crepitant collision between them.

This dropsy of the vesicle may attain any degree; it may become enormous when a calculus at the neck of the bladder acts as a valve and allows the bile to flow in but none to escape. Cases have been cited in which such tumors were taken for ovarian cysts or for ascites. I once published a case in which such an enlargement of the gall-bladder was taken for an extra-uterine pregnancy that had moved high up in the abdomen. These aseptic biliary tumors have a general tendency to gradual decrease in size. Their walls undergo atrophy and sclerosis, and little by little is produced the obliteration that is the rule in old cases of cholecystitis.

The third class of tumors of the right hypochondrium, that of the tumors of the large intestine, and particularly of the subhepatic angle of the colon, also deserves our attention. They are almost always neoplasms, and, although their pathologic anatomy is well known, their clinical signs are less understood. When we find alternating diarrhea and constipation, or increasing constipation, bloody stools, and melena, a diagnosis is not difficult; and then, if we can find a tumor of the subhepatic angle of the colon,—since that it is the region with which we are now dealing,—there can be no question as to the disease. But the situation is not always so simple. There are obscure cases that manifest themselves solely by little crises of intestinal strangulation. In addition, these tumors may cause great trouble, physically, as to their origin, as they may be dull and more or less movable, according to their adhesions. Finally, they may, at the outset, be extremely small, nothing more than a cancerous ring, and be hidden by abscesses deep in the abdomen to which they have given rise. Last year I published several instances of this sort, and such cases, which had not previously been reported, are common, to judge by the many corroborative examples that have since been cited. You have only to recall the man in our wards, who appeared to have merely an ordinary abscess of the iliac fossa, due to subacute appendicitis, but which we found to be the first indication of a cancer of the ascending colon. A blood-count alone enabled us in that case to foresee the nature of the disorder, as it was not at all that of a case of deep suppuration.

I have now come to the conclusion that beyond the age of 50 all acute intestinal obstruction is due to cancer; by applying this rule, which is clinically exact, you will not be mistaken very often.

Finally, mucomembranous enteritis may also give rise to tumors of the right hypochondrium produced by the contracted intestine. Beside the functional signs that help you in your diagnosis, the physical examination of the abdomen is here of great importance. If you palpate the iliac region and lumbar fossa of these patients you find an irregular, hard, and painful cylinder exactly in the line of the cecum and ascending colon. This cylinder is movable transversely, but not vertically; its size cannot be made to vary, and, as a rule, you will find a similar one in the region of the sigmoid flexure on the opposite side. If you wait for the painful crisis to pass, and examine the patient again during a period of calm, you will obtain splashing sounds over the cecum, proof of its dilatation; then, when a fresh crisis occurs, you will once more find a short, hard, rounded cylinder in the same iliac fossa. In many cases these painful attacks exist in patients with a floating kidney, which will sometimes be found higher up than the iliac tumor; they are one manifestation of that common condition consisting in congenital weakness of tissue,—weakness of the abdominal wall, visceral ptoses of different kinds, and gastro-interstitial lack of tone,—to which I so often call your attention.

To these elements of clinical diagnosis between the tumors of the right hypochondrium should be added various clinical methods and laboratory tests, which, although having no absolute value, may yet, in many cases, help out an uncertain diagnosis.

First, the distention of the colon by an enema, or by a mixture that will generate gas; the change effected in the zone of dullness and of resonance will perhaps enable you to assign the tumor to its true origin. Next, the test for cholemia, according to the method of Gilbert and of his followers. Again, a blood-count, which is often of great importance in these cases. Finally, the division of urine, together with its bacteriologic and microscopic examination, will be of considerable assistance to you.

You will now have an idea of the difficulties connected with the diagnosis of subcostal tumors of the right side. I have gone into the subject to show you that in practice, by minute and methodical analysis of the symptoms and of the causative data, combined in certain cases with laboratory tests, you will, in the majority of instances, reach an exact diagnosis, and, thereby, a rational treatment.

Neurology

ACUTE ANTERIOR POLIOMYELITIS, WITH SPECIAL REFERENCE TO THE STAGE OF INVASION

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ACUTE anterior poliomyelitis is one of the most common of the acute organic diseases of the nervous system. It may be conveniently divided into four stages, which in most cases are readily distinguished: (1) The stage of invasion, (2) the stationary stage, (3) the receding stage, and (4) the residual or permanent stage.

The first stage comprises the period elapsing from the appearance of the first general symptoms until the paralysis has attained its greatest severity and widest distribution. The second stage is reckoned from this time till the paralysis commences to subside. Then comes the third stage, which terminates, when there is no longer any improvement, in the fourth, or permanent, stage.

The purpose of the present communication is to direct attention mainly to the first stage, because this may present such a diversity of striking symptoms, or may be so devoid of these that the practitioner may find himself sorely perplexed in the former, and sadly surprised in the latter case in trying to reach a diagnosis.

The physician perceives plainly that his patient is suffering from an acute infectious process of some kind; but he is surely to be pardoned if he fails to suspect its true nature, for until paralysis makes its appearance, no pathognomonic symptoms are seen; furthermore, though acute anterior poliomyelitis is relatively frequent as a disease of the nervous system, it is very infrequent as compared with the cases encountered in general practice. It is true epidemics occasionally occur when a score or more cases of the disease develop within a radius of a few miles, yet it very often happens

that a practitioner does not have an opportunity to study the earliest stage of the malady in more than two or three cases in the course of a lifetime, and these separated perhaps by long intervals. Thus, it will readily be understood, if the stage of invasion presents symptoms widely at variance with standard text-book descriptions, while at the same time the paralysis may be quite unusual, either in regard to its distribution or severity, or both—it never presents any variation as to quality, being always flaccid and atrophic—the diagnosis may be reached rather tardily.

A perusal of the following clinical reports may happily give the practitioner a somewhat broader view of this class of cases, and cause him to consider more than heretofore the possibility of any acute infection he may be called upon to treat, having a specific incidence finally upon the bodies of the peripheral motor neurons—of its being, in fact, the stage of invasion of acute anterior poliomyelitis.

CASE I.—Rather Unusual Distribution of the Permanent Residual Atrophy.—A. C., a girl of 3 years, previously healthy, became restless and feverish during the night in September and vomited several times. The temperature was 101° F. Toward the next evening the child was more comfortable, walked about, and occupied herself with her playthings. During the night she began to complain of pain and soreness in the arms and legs, and cried out if moved or touched. On the morning of the second day it was noticed that there was complete flaccid paralysis of the arms, legs, and neck, but that sensation was not impaired. By the fourth day all signs of fever were gone; the pain and soreness were less, and there was some return of power in the legs, less in the right arm, and none in neck and left arm; but in the course of a few weeks slight power of movement appeared in these last-mentioned parts, more particularly in the forearm and hand.

Six months later a practically permanent condition had been reached. The paralysis and wasting are marked in the left side of the neck, trunk, shoulder, and upper arm. There is considerable anterior and lateral flexion of the dorsal spine as the child sits or stands, and she cannot rise from the ground without assistance when lying flat. In this case, then, there was considerable destruction of neuron bodies in the anterior horn of the left side, extending from the upper cervical cord to the mid-dorsal region, whereas it

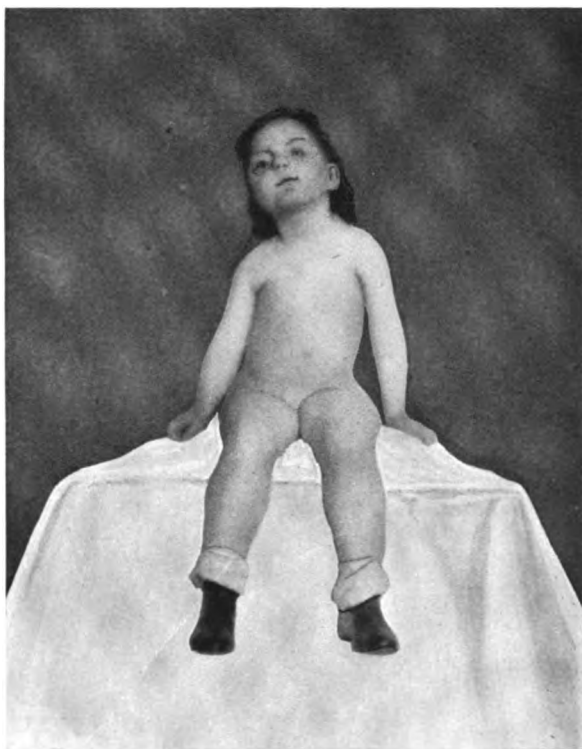


FIG. 1.—Residual atrophy and paralysis after acute anterior poliomyelitis.

is well known that in the vast majority of cases the permanent injury is limited to the lumbar enlargement (Fig. 1).

CASE II.—*Stage of Invasion simulating Meningitis; Long Period of Intermission.*—F. B., a boy, aged 4 years, was always rather delicate. In August, when two and one-half years old, he appeared to be suffering from a bad cold, and when riding in a carriage complained that the vibrations caused abdominal pain. After suffering in this way for two days, he went into a stuporous state, which also lasted two days, during which time he could be roused enough to drink. When natural consciousness returned, the upper extremities were seen to be paralyzed, the right more severely than the left. Presently he began to scream and dig his head backward into the pillow, as if in great agony. This he continued to do for nearly two days, before he began to show signs of getting easier. He was now quite comfortable for six days, when the legs also became rapidly powerless, the left to a greater extent, and a few hours earlier than the right. Pressure or movement of the paralyzed parts never caused pain, nor was there any sensory or sphincter involvement. No temperature record was kept, but the mother did not think there was a very high fever. The weakness began to recede a few days after it had attained its maximum, and at the time of my examination, 18 months later, the shoulder muscles were considerably atrophied, the right much more than the left, while in other parts recovery appeared to have been complete.

CASE III.—*Pons Involvement; Pseudo-Crossed Paralysis; Remission in Stage of Invasion; Suddenly Fatal Result.*—F. R., a boy of 3 years, previously healthy, had indigestion, and vomited Wednesday night, without obvious cause. He appeared a trifle feverish, but was about the house on Thursday, but not as lively as usual; toward evening a clonic spasm developed on the right side of his face, and a flaccid paralysis of the left arm and leg, more marked in the arm. The mother thought the arm was somewhat powerless before the spasm appeared in the face, but there was some conflict of testimony on this point. The temperature was 100° F., and the pulse and respiration not much disturbed. The mind was clear, and there was no sign of pain or sensory disturbance. On Saturday morning, when I was called, the condition was essentially as described, but on being tested for the first time no skin or tendon reflexes could be elicited. The

temperature had been 101° F. during the night. The facial spasm would occur several times a minute for five minutes, then intermit completely for a few minutes, and so on for about a half hour, when it might not return for an hour or more. Each separate contraction came on deliberately, remained for a few seconds, and passed off slowly; there was no jerking, and the child would give his attention to things about him while the spasm was taking place. At the height of the spasm the eye was closed firmly and the angle of the mouth drawn upward and outward. I could not determine any deviation of the eyeball. During the next few days the child appeared quite comfortable, the temperature ranging from 99° to 100° F., and the facial spasm having gradually subsided; but on the seventh day of the disease, after suffering about an hour from embarrassment of respiration, death occurred, without convulsions.

In this case, as in the former, there was probably a partial remission in the period of invasion, and when activity was resumed the respiratory centers in the medulla were attacked by the infective process.

This case presented some features which might lead one to think of a lesion—a small hemorrhage—in the pons, producing irritation of the fibers of the facial nerve, and at the same time injuring the fibers of the pyramidal tract prior to their decussation. Had this been the fact, however, the paralysis of the leg and arm would have been spastic. That is to say, it would have been an upper segment paralysis. The course was quite consistent with the stage of invasion of acute anterior poliomyelitis. Furthermore, a hemorrhage sufficient to produce the paralysis present might be expected to produce more or less profound symptoms of apoplexy at the time of its occurrence—indeed, a fatal result would be most usual.

CASE IV.—Stage of Invasion simulating Acute Articular Rheumatism.—This case occurred in the practice of Dr. J. H. Copenhaver, Bellflower, Illinois. W. K., a boy of 16 years, was always healthy. On the morning of October 8 he felt very languid and had no appetite; but he kept about at farm-work until toward evening, when his temperature was 102° F., and he complained of quite severe pains in the knees. On October 9, the pain in knees was very severe during the night; he was restless and slept little. On the following day the pain left the knees and went to the shoul-

der; there was profuse sweating. The temperature was 102° F. In like manner the intense pain in the joints continued to shift; the temperature varied from 100° to 102° F., and there were frequent profuse sweats for nearly two weeks, at which time the patient regained his appetite and became comfortable.

On the third day of the fever it was noticed there was complete loss of power in the left leg, except that the great toe could be moved ever so little, and slight outward rotation was possible. Two days later the other limbs were similarly, but not so severely, affected, the right leg more than the arms, but the latter were entirely useless. At the end of two days improvement set in, and in three weeks he had regained considerable power in the upper limbs, less in the right leg, and least in left. There was no improvement of sensation at any time, nor were the sphincters affected.

On January 25, the date of my examination, nearly three months from the onset, power in the upper extremities was normal; there was very little power in the left leg, with marked atrophy and degeneration; the muscles below the knee reacted to the electric current, but less above the knee. The right leg was affected in the same way, but not so severely.

If the single symptom of paralysis is excluded the clinical history of this case is singularly like that of acute articular rheumatism. Indeed, if one wished to argue that it was a case of the latter disease, complicated with acute anterior poliomyelitis, the contention could be quite plausibly maintained. It is true, however, that severe joint pain is found in other infections—pneumonia, gonorrhea, and typhoid fever, but rarely, except in acute articular rheumatism, does it cease so quickly and completely in one pair of joints to attack another pair, shifting in the way it did in this case, from day to day, nor is it likely to be accompanied by such regular attacks of profuse perspiration.

CASE V.—*Acute Nephritis; Stupor; Rectal and Vesical Sphincters, Cardiac and Respiratory Centers Involved.*—C. B., a boy of 16 years, was a professional juggler, mainly with Indian clubs; of correct habits, and good family history. He has always enjoyed good general health prior to the present illness, which was as follows: On the morning of October 16 he had a slight headache and felt somewhat indisposed generally, but did his turn at the theatre in the evening as usual. He slept very poorly

during the night, and experienced considerable pain in lower limbs from hips down, and noticed that he could move them in bed only with considerable effort. On attempting to rise on the morning of the 17th the legs were found to be entirely powerless, and he was unable to void his urine. He was admitted to St. Luke's Hospital, October 20, and in the meantime, excepting for the pain in legs, which was not very severe, he had not suffered much, though he had slept poorly, bowels had not moved, urine had to be drawn with a catheter, and his legs had continued entirely motionless.

On admission: Intelligent, well-developed boy; complete flaccid motor paralysis of legs, with some sensitiveness to pressure, and pain in joints on movement, but no impairment of sensation. There was marked paresis of the upper extremities, though all desired movements could be feebly made. The urine was loaded with albumin, and there were abundant granular and hyalin casts. He entered the hospital at 9 A.M., complaining of slight malaise, and some pain in legs only. Temperature, 100.6° F.; pulse, 84; respirations, 20. The record showed a gradual increase till 9 P.M., when it was: temperature, 102° F.; pulse, 104, and respirations, 44. There was an involuntary bowel movement after magnesium sulphate and a high enema. Complete incontinence of urine.

October 21. Fifth day of disease. Very restless and slept little; looks worn and anxious. Several involuntary bowel movements. Complete incontinence of urine; normal quantity passed per catheter. Temperature, 99.8° to 101.4° F.; pulse, 86 to 108; respirations, 20 to 32. Very restless. Condition of urine same as yesterday.

October 22. Sixth day of disease; restless and slept very little last night. Bowels and urine reported same as yesterday. Temperature, 100° to 100.6° F.; pulse, 72 to 96; somewhat irrational and dull mentally at times.

October 23; seventh day. Slept fairly last night. Temperature, 98° to 101.4° F.; pulse, 68 to 88; respirations, 18 to 24. In light stupor most of day. Several involuntary bowel movements. Urine in normal amount drawn with catheter, but it contained very little albumin, and few casts.

October 24; eighth day. Slept well. Temperature, 98.2° to 99.2° F.; pulse, 64 to 80; respirations, 20 to 32. No note of mental state. Passed urine for first time with involuntary bowel movements. Urine showed no casts and only a trace of albumin.

October 25; ninth day. Slept well. Temperature, 98° to 99° F.; pulse, 64 to 76; respirations, 20 to 28. Comfortable, mind normal; stronger in hands and arms. Complete flaccid paralysis of legs; no pain, and only very little tenderness in them. No sensory impairment anywhere at any time. Urination and defecation under voluntary control from this time on.

The further progress of the case, until the patient left the hospital, January 6, nearly three months from admission, presented no unusual features. In the course of a few weeks the pain and tenderness had entirely vanished from the legs, and he had regained natural power in the arms and hands. In the lower limbs power was first regained in the hips and thighs. When he left the hospital he could not, lying on his back or side, flex the knees or ankles; he could change the position of the pelvis and move the great toes slightly. The muscles showed marked atrophy.

The urine, otherwise normal, continued to show a fraction of 1 per cent. of albumin pretty constantly, until December 24, but none thereafter.

The unusual features of this case are: (a) The age of the patient; (b) the season; (c) the involvement of the sphincters; (d) the mental symptoms; (e) variations in pulse and respiration, and (f) the acute nephritis.

Assuming that the main causative factor in the disease is a toxin circulating in the blood or lymph, or both, it would not be unreasonable to suppose that it had acted with unusual severity upon these neuron bodies comprising the vesical, rectal, cardiac, and respiratory centers respectively, and also on the cortical neurons concerned in mental operations, because there was not sufficient elevation of temperature to account for the mental changes.

Nephritis may be accounted for by assuming the development of a renal irritant, as in other acute infections—scarlet fever, measles, etc. I do not think it need be seriously considered as a cause.

An examination of the year-books on neurology extending over several years discloses cases in which the acute stage of acute anterior poliomyelitis has presented various anomalies and complications no less striking than those here recorded, but it is not probable the practitioner may encounter them so frequently in current literature that the above descriptions may fail to be of some interest and value to him.

PARALYSIS AGITANS; HEMIPLEGIA; COMBINED SCLEROSIS AND ATAXIC PARAPLEGIA; LOCOMOTOR ATAXIA; ACUTE CONFUSIONAL INSANITY

A CLINICAL LECTURE DELIVERED AT THE COOK COUNTY HOSPITAL

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PARALYSIS AGITANS

GENTLEMEN: I wish you to notice the gait of this man as he approaches us. Observe the tremor. He walks with the center of gravity well in front. The same is true of the other man near him. I call your attention to the fact that the tremor is fine; it is not coarse like that of St. Vitus's dance. It is rhythmic and constant. Movements do not exaggerate the rhythm, but rather diminish it. That is an important point. As he places his hand upon his leg in repose the movement is vigorous; as he brings the hand up to his nose the tremor diminishes. It is not increased by voluntary movement. The other patient does the same thing. The tremor is practically all gone from the hand during the movement of bringing the hand to the nose. It is therefore not an intention-tremor. An intention-tremor, as you doubtless know, is one that is manifest on movement. The hand may be perfectly still, but just the moment a purposive movement is undertaken the tremor comes on. These cases, then, have a peculiar kind of tremor—fine in character, regular in rhythm, and not increased by purposive movements. If we attempt to move the arms of these patients, we will find there is a certain amount of rigidity. Muscular power is greatly diminished in the hands of these patients. As the patient squeezes my hand the tremor almost ceases, which is another evidence that it is not intentional.

This patient is 64 years of age, and two years ago he noticed a tremor in the right hand. It was fine at first, but gradually became coarse, and in time the left upper extremity became involved.

Secondarily, the tremor began in the right hand, where it ought to begin. This is a case of paralysis agitans. I will show you later on some intentional tremor cases.

Until the great Charcot differentiated these from ordinary insular scleroses, we called them all paralysis agitans—shaking palsy. Charcot taught us to differentiate them, and his essential point of difference was that the tremors are not intentional. We differentiate these cases by the absence of intention and by the peculiar kind of tremor. It usually begins in the right hand and with what may be called the “pill movement.” In olden times, before the days of pill-machines, the druggists made pills with their fingers. Frequently this pill movement may be manifest for many years before we get the general disturbances that we have in the two cases before us. One of the most interesting cases of paralysis agitans I ever had was that of a druggist, quite a celebrated man, and I think a word or two about his history will be of interest to you. He was a young man comparatively, only 45 years of age, while one of these men is 64. Paralysis agitans does not usually begin before the fiftieth year. It began in the case of the druggist at 45. His wife had been an epileptic for many years. He had heard of a new cure for epilepsy; some new doctor had come to town and made him believe that he could cure his wife. She had been previously treated by many physicians without any benefit, and her case was regarded as incurable. He heard from this physician that gelsemium would cure her; and in order that he might have the benefit of the best possible preparation he sent to a Cincinnati house that was making a specialty of such remedies. He obtained a new and strong preparation. Some preparations of gelsemium are without any medicinal properties, while the stronger preparations of the green root are powerful. He gave her twenty drops, and after a certain interval twenty drops more, supposing that the drug was exerting its quieting effects on the patient, until finally he gave her so much that she could not be aroused, and she died. The shock of his wife's death was terrific, because he felt he was responsible for it, and not the doctor who had prescribed the drug. Two or three months after the death of his wife I was in his store, and he said to me: “Doctor, I am constantly making the movements I used to make years ago when making pills; I find myself going through the pill movement.” This was the beginning of his paralysis agitans. The

disease continued to advance until eventually he died. This disease goes on increasing in intensity, particularly the paralytic symptoms, until the patients become bedridden.

We can diminish the progression of the disease in some cases, but we cannot cure it. Paralysis agitans is due to two things. First, to degeneration which takes place in the blood-vessels in the spinal cord, the medulla, and possibly of the brain; second, to changes that take place in the nerve-cells in the brain and spinal cord, and to an hypertrophy of the neuroglia.

I have here some pictures showing the changes that take place in the spinal cord in cases of paralysis agitans. It is supposed to be in its essential basis the product of some toxic, infectious process, the precise nature of which we do not know. The disease makes such inroads into important parts of the nervous system, as the blood-vessels and cells, that there are no drugs that can cure it. But we can diminish the rate of progression of the disease by enforcing rest. I have a few patients who are making good headway by what is known as the rest cure. Periodically, usually twice a year, they go to bed, and are put through the rest cure for eight weeks. I refer to the Weir Mitchell rest cure, which consists of absolute rest in bed, massage, electricity, careful feeding, and strict attention to elimination. After the expiration of eight weeks patients begin to resume their ordinary avocations. In the interval between the rest cure we give one of the nerve tonics, as the phosphid of zinc, syrup of hypophosphites, and to diminish the tremor we administer hyoscyamus, or the hydrobromate of hyoscin. These are among the best agents we have for this disease. We may give one full dose of the tincture of hyoscyamus, or its extract, or the hydrobromate of hyoscin at bedtime, with some tonic during the daytime, and every now and then with a long period of rest we can diminish the rate of progression of this affection, and do much toward prolonging life.

LEFT-SIDED HEMIPLEGIA

This patient is 70 years old. A few days ago he slipped on a banana-peel and fell, striking the sidewalk with his shoulder but not his head. On attempting to get up he fell backward, striking the ground with his occiput. He did not lose consciousness; he was unable to rise, and found himself unable to move either the left leg or arm. He suffered from pain in both the lumbar and posterior

cervical regions. He had no disturbance of the special senses, but he did have a ringing in the left ear. Power in the left arm and leg was greatly diminished for a time, but two days ago he began to move the fingers of the left hand and to flex them, but he has lost grip in that hand. At the present time he has almost entirely regained the power of this hand, although the leg is still impaired. He has never had an attack similar to the present one. His only recent illness was an attack of la grippe. He comes from a long-lived family. There are some defects in the family history. One sister died of tuberculosis, one was epileptic, and one had a large abdominal tumor removed. A brother died of cerebrospinal meningitis, while another brother died at the age of 20 years. The cause of death we do not know. This patient informs us that he has had rheumatism and gonorrhea, but not syphilis. He drinks moderately, and smokes to excess. There is no exaggeration of either the patellar tendon or of the plantar reflexes. He has very marked arterial degeneration. His case is one of left hemiplegia.

RIGHT-SIDED HEMIPLEGIA

This man is 24 years of age, and his case is one of right hemiplegia. Power in the limbs is gradually returning. Up to within a few days ago the patient was said to be in perfect health, when he was suddenly seized with an apoplectic stroke. He fell and passed into a state of coma, and remained so for a number of hours, at the end of which time he regained consciousness. He found he was unable to use the right side of his body. There was aphasia in his case.

I want to call your attention to two points in which these cases differ. The man previously shown you had no aphasia; he did not lose consciousness. He did not have an apoplectic seizure. His paralysis is left-sided. Loss of the power of speech with left hemiplegia is very uncommon. We know that the speech-center is on the left side, and in this man's case the lesion is on that side. Another interesting contrast between the two cases is that one is 24 and the other 70 years of age. A man at 24 ought not to be paralyzed.

The basis of cerebral paralysis ninety-nine times out of a hundred is circulatory, due to embolism, thrombosis, or hemorrhage, occasionally to congestive apoplexy. I want you to observe the

very important point that there is almost as much arterial degeneration in this man's case at 24 as there is in the other at 70, and "a man is as old as his arteries." I do not know whether this man of 24 admits a luetic history or not. He now tells us that he had a chancre. With this condition of the arteries, in the absence of renal disease, we are justified in giving iodid of potassium. The man of 70 is improving very rapidly. The hemiplegia in the man of 24 is of syphilitic origin. He is taking 60 grains (4 grams) of potassium iodid four times a day. This is good treatment, and such cases call for the heroic use of the iodids.

COMBINED SCLEROSIS AND ATAXIC PARAPLEGIA

Let us compare the two patients. This man has almost as much difficulty in standing up as the other case. His sickness began 6 years ago, at which time he felt pain in the legs, and his muscles would cramp. These pains were very sharp and lancinating and of short duration, but recurred frequently. It is exceedingly difficult for him to stand with his eyes shut. You will notice that the character of the sensations in the two patients is different. In the man we showed you a moment ago there were ill-defined sensory disturbances; but here, in the man before us, we are told that the pains are sharp and lancinating and of short duration, recurring frequently. The symptoms have increased in severity during the last four or six months, and the patient informs us that for a time, about a year and a half ago, he had considerable difficulty in walking. His eyesight is failing. His pupils are very much contracted, while in the other case they were dilated. There seems to be no response whatever to light. He has had both gonorrhea and syphilis; the other patient denied a history of either of these diseases.

Let us learn the condition of the reflexes. In this case we notice that there is practically no patellar-tendon reflex on either side, and consequently no ankle clonus. In testing this man to find out whether he has much strength in the lower extremities, I find that he has considerable power in the limbs. We notice a difference in the character of sensory disturbance in the two patients. There is a marked difference in the reflex manifestations. The amount of ataxia seems to be equal in both men. One is a case of combined sclerosis and ataxic paraplegia; the other an ordinary, but rather

rapidly progressive, case of posterior spinal sclerosis, or locomotor ataxia. The disease in one is limited to one column of the spinal cord.

We have here a diagram of the spinal cord which will assist us in determining what portion of the cord is involved. In the case of locomotor ataxia we will examine for the plantar reflex. If he has this reflex, then both columns of the spinal cord are not involved. This is an important point to determine in making a prognosis in locomotor ataxia. You doubtless noticed that he made a slight voluntary movement of the toes; there is no reflex response from the irritation, and the movement of the toes was purely voluntary.

By looking at this diagram you will see that the superficial reflexes extend into the posterior horns, the column of Goll; the patellar-tendon reflex goes into the column of Burdach, but inasmuch as the patient has no plantar or patellar-tendon reflex, we know that both posterior columns are included in the pathologic process in this case.

In the other case we not only have sclerosis of these columns to account for the sensory symptoms, but a very much greater degree of sclerosis in the crossed pyramidal tract in this lateral column to account for the exaggerated reflexes and diminished muscular power. So we have both the lateral and posterior columns invaded in one case, and only the posterior columns involved in the other.

LOCOMOTOR ATAXIA

This man is 35 years of age. Two years ago he began to experience pricking and tingling sensations in the left arm, and since then the right arm has become involved, as well as both legs, so that now he feels these sensations all over the body. He informs us that both legs are becoming weak and stiff. His bowels are unusually constipated. For the last two months he has been compelled to get up once or twice during the night to urinate. For the last three or four days he has been passing urine in small amounts. Hearing, smelling, and tasting are normal. He tells us that four years ago he passed through a severe financial trouble; he worried a great deal, and he has lost twenty-five pounds in the last year. The patient's sister says that he has been irritable and abusive to his family. His father died at the age of 70, his mother at 83 of blood-

poisoning after a broken arm. He has a brother and two sisters living. His wife has borne seven healthy children, all of whom are living. She has had no miscarriages. The patient has had malaria and cholera morbus. He denies a venereal history. He has been a moderate drinker, but an excessive smoker. His pupils are unequal, the left being much larger than the right. Both are dilated, but one is more so than the other. The pupillary reflex is greatly diminished. The facial muscles seem to be normal. In examining the legs we find the patient has some paresis as well as some disordered sensations. Tactile sensé is impaired, as is also pain sense. Sensation seems to be better in the upper than in the lower extremities. We observe a very lively patellar-tendon reflex on both sides. The same is true of the plantar reflex. There is very marked ankle clonus on the right side. In making an attempt to bend the limb I find there is considerable rigidity. We have in this a case a combination of sensory and motor disturbances, and associated with them exaggerated patellar-tendon reflex and ankle clonus. You will notice that the ataxia is more marked with the eyes closed.

ACUTE CONFUSIONAL INSANITY

We have here two cases of mental disease. It does not require any statement or explanation from me to satisfy you that the patient in bed is disturbed in mind. A simple glance at the features, or physiognomy, will influence our diagnosis of mental disease. The study of physiognomy is very much neglected to-day when we have all of the instruments of precision in diagnosis, such as stethoscopes, otoscopes, etc., etc., and I think we are disposed to neglect those things which our forefathers in medicine regarded of so much importance. If you read the older text-books on practice, you will find great stress laid upon facies, or physiognomy, of disease. We have in this woman in bed a facies that you cannot mistake. There are unmistakable lesions showing mental deterioration with mental enfeeblement. To use a common expression, this woman looks silly, idiotic. She is demented. The other patient, the woman in the chair, has improved to such a degree that she does not show very markedly the physiognomy of mental disease, and yet I have had her brought to the amphitheatre as a most interesting case of mental disease with which you should be familiar, because it is not an uncommon form of insanity. Her face appears

to-day as it did when I saw her a day or two ago, there being evidence of mental depression, although during the greater part of the time for the last month she has been in a state of mental agitation with a great deal of mental confusion. She was admitted to the hospital not as a case of insanity (neither was the other one), but as a case of typhoid fever, and shortly after her admission it was found that she had more than the usual amount of coma that we observe in patients with typhoid fever to-day, but no more I fancy than I saw when I began the study of medicine, because typhoid-fever cases have changed with respect to the development of mental symptoms. There is much less coma and delirium in cases of typhoid fever to-day than there were twenty years ago, for some reason or other.

She came into the hospital as a case differing from the ordinary run of typhoid-fever patients, in that there was more delirium and more coma than we usually see accompanying cases of typhoid fever. The first temperature record was 104° F. The febrile condition continued for two or three weeks, but by the latter part of June the fever had practically disappeared. On the 30th of June the temperature was normal in the morning at 8 o'clock. It was practically normal from that time on, and she has had no elevation of temperature since. When the fever had left her she began to show mental disturbance. She was in a state of confusion of mind, so that she could not talk. She is a Swede, and because she could not make her wants known or could not answer questions intelligently, the idea was entertained that she could not speak the English language. She speaks the English language as well as we can expect. Later on she became so violent that it was necessary to restrain her, and this violence continued up to within a few days ago. I believe it was on Tuesday or Wednesday night that I saw her for the first time, when she was not so quiet and composed as she is now. At that time I could not get her to tell me her name or to answer any questions that I put to her. She has so far improved that she now gives a fairly intelligent and prompt answer to my interrogatories. Her comprehension, however, is not fully established yet. You see clearly that there is yet some mental disturbance. It is a case of post-febrile insanity, frequently called, and by the more recent authors, acute confusional insanity.

The other case is one of insanity due to organic brain disease.

The case of post-febrile insanity is of interest for several reasons. First, it is a form of insanity due to intoxication; cerebral exhaustion from the presence of toxins of typhoid fever is the foundation. Very many of the insanities are due to intoxications, and the more the etiology of insanity is being studied, the greater will be the number of cases referable to intoxications. The toxins of any of the infectious diseases may bring about this condition. A form in which many cases of insanity begin is called melancholia, because it was supposed in the beginning, and we believe it can be established by our knowledge of to-day, that melancholia is due to some derangement of the chylipoietic viscera. It was named melancholia because it was supposed to be due to some disturbance in the biliary secretion. This is an intoxication from the toxins developed from germs from without.

This patient with post-febrile insanity is pursuing the course that these patients usually pursue, namely, she is getting well. Such patients can be treated in ordinary hospitals, or at their homes. Unless the surroundings are most unfavorable, there is no reason why they should not be treated at home. The acute confusional insanities, the product of intoxications, can be treated, as a rule, at home. Surely, they can be treated in general hospitals, such as we now have scattered all over the country, in almost every flourishing town.

As they are largely cases of brain exhaustion the product of intoxicating agents, the indication for treatment is elimination. We must get rid of the intoxicating products as rapidly as possible; we must promote elimination by the bowels, by the skin, and by the kidneys, and it behooves us to determine which of the organs of elimination is deficient. If there is great deficiency in the bowel, then the patient must have laxatives, and those of the greatest value are the preparations of aloes. An admirable combination for this purpose is the extract of aloes put in with a little pulverized ipecac, which intensifies the action of the aloes and secures a better action on the part of the liver. We may add to it a little hyoscyamus. Hyoscyamus will prevent the griping effect of the aloes, and it is a good sedative to the nervous system, in that it will diminish the hyperesthetic condition of these patients.

We must study the urine. If urinary elimination is deficient, as it is very often in these cases, we must stimulate elimination by

the kidney, and there is, as a rule, no better stimulant for this purpose than the citrate of potassium or some other one of the potassium salts. The citrate of potassium or bitartrate of potassium may be given once or twice a day. The bitartrate of potassium may be given (say a teaspoonful) in lemonade without changing its taste. This will secure good action of the kidneys. The skin is very often sluggish and very dry. You can promote its activity by massage better than by any other way.

Next to securing proper elimination in the post-febrile or acute confusional insanities it is important to increase the general tonicity. Tonics are indicated, and it becomes us to determine the blood record of these cases. We will usually find a deficiency in hemoglobin, and this is always an indication for the administration of iron. I have a great partiality in my own practice for Blaud's mass. Blaud's mass consists, as you remember, of carbonate of potassium and the sulphate of iron. This will meet the iron indications in such a case.

There are other indications to be met in cases of post-febrile insanity. The pulse may be very quick, but it is usually compressible, whence there is necessity for giving a cardiac stimulant, as well as a stimulant to the nervous system generally. In this event *nux vomica* may advantageously be added to the iron, as follows:

R	Potassium carbonate		
	Iron sulphate, of each	2 grains	0 13
	Extract of <i>nux vomica</i>	$\frac{1}{2}$ grain	0 015
	Mix, that is, rub up dry, and make one capsule.		
	Sig.—One such capsule three times daily.		

There is one other indication to be met, and that is insomnia. Occasionally we meet with cases of acute confusional insanity in which the patient is in a stuporous condition, but almost invariably there is necessity for the administration of some sleep-producing agent. In selecting a sleep-producing remedy we must not use anything that is very depressing, because the whole phenomena of the case is the result of depression. We must avoid remedies that have a very bad taste. Our prescriptions must be put up in a liquid form and made agreeable. By employing sulphonal in 15- or 20-grain doses (1 to 1.3 gm.), which is practically tasteless, we can sometimes produce sleep. We will more surely produce sleep by adding to it hydrobromate of hyoscin. Such a patient as this might

take $\frac{1}{100}$ grain (0.00065 gram) of hyoscin hydrobromate, given in a glass of hot milk, which will readily dissolve the sulphonal and have no taste. It can be given in powder form, mixed with water, and thus rendered tasteless. So much for the internal medication of a case of ordinary acute confusional insanity.

There is something more important than drug treatment, and that is feeding. These patients require a great abundance of easily digestible food. The ideal food for such a patient is eggnog. She may be given five or six eggnogs a day. I have repeatedly given such patients that number of eggnogs daily; that is, in twenty-four hours. In addition, we should give such other foods as we can induce them to take. She could manage now food that requires chewing, but a week or ten days ago if we had given her beefsteak it would have been bolted. She would have failed to receive the maximum benefit of nutrition, so that during the active manifestations of acute confusional insanity patients should have liquid foods. We can give them meat-juice, raw eggs, milk, koumiss, and a host of similar foods. If the eggnogg is distasteful, we must find some other food that is equally nutritious and give it in great abundance.

During the active manifestations of the disease it is wise to keep the patient in bed. As the improvement continues, she should have a reasonable amount of exercise. As soon as possible she should be given some occupation, and just as soon as we can induce her to do some sort of work, we can get her on the road to recovery.

Dermatology and Syphilology

SYPHILITIC NECROSIS OF THE FRONTAL BONE

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THE subject of syphilology is far from being exhausted, despite the enormous amount of literature which has been devoted to it since the fifteenth century. The modern trend of study has been to consider special subjects in connection with the disease, such as treatment, pathology, special points in symptomatology, more advanced methods in diagnosis, the inoculation of animals, the more specialized nervous troubles and disturbances owing their origin to syphilitic infection, and a host of other equally interesting and important topics. The investigators and delvers have permitted no organ or tissue to escape their scrutiny and research, and still the end is not yet. What has been done is little when compared with what remains to be done.

Among all these there is one condition which has had considerable attention paid to it—syphilitic affections of the bones. Much has been written upon the bony involvements observed in syphilis, from the lesions observed in infancy to those seen in old age, including the periosteal changes due to syphilis. And yet, in all of this literature, which is large, there appears but little or nothing on the condition which it is here proposed to be discussed. This would seem rather strange in view of the fact that it is of comparatively frequent occurrence and the objective as well as subjective symptoms are sufficiently prominent to call attention and awaken an interest in them. On the other hand, some considerable attention has been called to necrosis of the skull, but the frontal bone has not been particularized.

Several cases that I have lately seen suggest my calling attention to the condition :

CASE I.—William W. was admitted to the St. Louis City Hospital, May 24, 1903. He was 45 years old, a shoemaker by occupation, and unmarried. He could not tell the cause of his father's death, his mother was living, and brothers and sisters were healthy. (It may not be inappropriate to mention here that his mother eventually died of senility.) He was in the enjoyment of good health during his childhood, with the exception of an attack of measles, until he attained his fifteenth year. It was then that he had an accident to his left knee, which resulted in an arthritis, having the symptoms of a tubercular joint affection. The knee was not treated, but the process was permitted to run its course. This resulted in an ankylosis and contractures, necessitating the use of a crutch, which he still employs. He contracted gonorrhea for the first time at the age of 20 and again later. When 26 years of age he noticed, after a suspicious intercourse, a papule on the prepuce. Being alarmed at this manifestation he cauterized it with pure carbolic acid. The lesion disappeared in such a prompt and complete manner that he did not deem it necessary to consult a physician. Some time after he became quite ill and had a macular eruption, which the physician whom he consulted pronounced syphilis. Under his treatment all subjective and objective symptoms disappeared. He then felt well and resumed his occupation and worked steadily at his trade. In 1891 he noticed a swelling forming over the left frontal eminence. This had a doughy consistence and became progressively larger and larger, and a physician whom he consulted cut it open, yellow pus being discharged. He drifted from one hospital to another and received treatment. He also went to the Hot Springs, of Arkansas, and experienced some benefit, but a relapse soon set in.

Upon his entrance into the St. Louis Hospital he was emaciated and weak. The tissues over the greater portion of the frontal bone were destroyed, the destruction even extending as far down as the right orbit. The entire lesion presented broken-down tissues, which were foul and had a putrid odor. The bone itself was necrosed and carious in several places. A small amount of pus discharged, but the discharge was continuous and completely saturated the bandages which were used. The diagnosis was properly formulated and the treatment consisted in placing the patient under a course of potassium iodid in doses of 2 grams (30 grains) three times a day, which was soon increased to a little more than 5 grams (75 grains).



FIG. 1.—Case 1, after healing had become established.

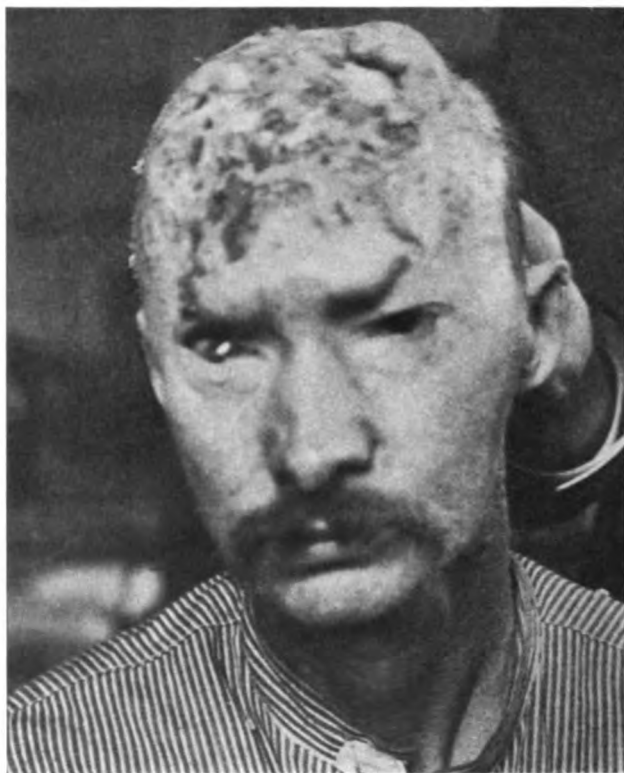


FIG. 2.—Case I. Front view of patient feeling comparatively well.

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FIG. 3.—Case I. Profile view showing loss of bone after operation. Note the necrosed bone above and behind the ear.

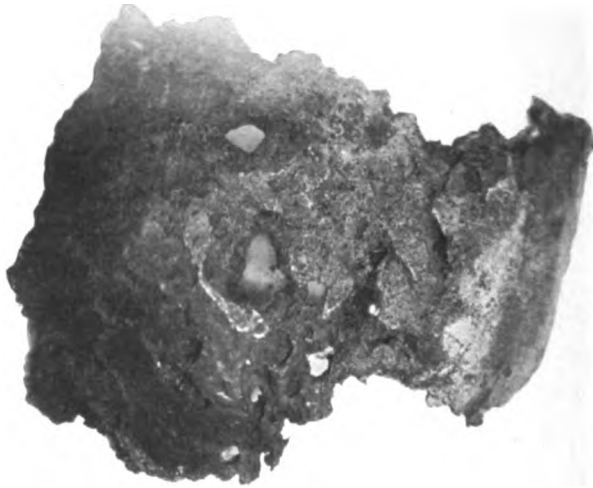


FIG. 4.—External surface of necrosed frontal bone removed from William W. (Case I), Nov. 16.



FIG. 5.—Appearance of Case II after removal of a portion of the frontal bone.

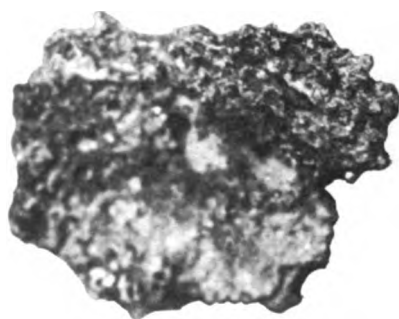


FIG. 6.—Internal surface of necrosed bone removed from Fannie M. (Case II).



FIG. 7.—Case III as seen at the St. Louis City Hospital, Aug. 10, 1896.



FIG. 8.—Case III as seen at Female Hospital almost in articulo mortis.

The condition remained unchanged until November 16, when resort was had to operative intervention. The entire necrosed portion of the frontal bone was removed, with little or no difficulty, in one piece, as shown in Fig. 4.

From this time on the hospital record is very incomplete. We find such entries as "improving," "the same," etc., but no indications of the treatment. I had the patient placed on mercuric bichlorid and potassium iodid alternately. He was enabled to go about for months at a time, when he became weak and was permitted to rest. The space formed by the removal of the frontal bone rapidly healed, and in time was protected by a thick resistant membrane of connective tissue and dura mater, as shown in Fig. 1, which is from a photograph taken after the healing had become established.

Figs. 2 and 3 illustrate the patient when feeling comparatively well. The left eye is destroyed and the sight gone, and there is marked necrosis of the left side, involving the parietal bone at its eminence. Latterly there was a severe trachoma and pannus of the right eye. The other bone lesions consist of a perforation of the palate to the left of the mesial line, complete absorption of the alveolar processes, perforation of the nasal cartilage, and some more small necrotic involvements of the skull.

CASE II.— Fannie M., aged 34 years, a housekeeper, had been married 13 years. She had three children, aged 4, 6 and 8 years, respectively. She had had two miscarriages. The first one was one year after marriage, three months after conception. Five years after her marriage she had a still-born child. Her family history is good. During the first year of her married life and three years after she was perfectly healthy, according to her account.

She first noticed a sore on her leg five years after her marriage. It is now chronic in character and lasted two years. Then it began to heal, and the patient enjoyed good health. About five years after (the time she was seen) there appeared a small lump on her forehead. This increased and became painful to a marked degree. The worst time that she ever had with her trouble occurred during the year previous to the time she was seen. The pains were diurnal and nocturnal, but worse at night. She presented a small round opening in her forehead, from which there discharged a thick, yellow fetid pus. The odor was distinctive of bone caries. Upon examining the

bone it was found to be necrotic to quite a considerable extent. Further inquiries elicited the history of syphilis, and the case was set down as one of syphilitic caries of the frontal bone.

Under these circumstances there was but one plan of procedure to follow, that of removal of the necrotic portion of the frontal bone. This was done without any untoward symptoms. The appearance of the patient after this operation is shown in Fig. 5. Whilst the bone removed did not embrace the entire frontal bone, it was considerable, and sufficiently attacked by the destructive process to justify the operative procedure, as may be seen from Fig. 6, representing the inner surface. The patient made an uneventful recovery and went home quite satisfied.

CASE III.—A married woman, 31 years of age, a housewife by occupation, was seen in the St. Louis City Hospital. Her family history was negative. She was first seen by the writer August 8, 1896, and she gave the following account of her previous history: When a child she had chicken-pox. Her present trouble began some five or six years ago, when she noticed a sore on her genitals. This was followed by a profuse rash over the body. The hair fell out very much, and all the symptoms of syphilis manifested themselves. Nocturnal pains in the tibiæ and violent headache were present.

In 1884 or 1885 she began the use of opium. She first learned to smoke it in a Chinese quarter, and later she ate opium in large quantities. She states that she was accustomed to eat several drams a day. She has never used hypodermic injections. In the winter of 1895 she began to cough. She has been losing a great deal of weight; has night sweats, which weaken her much.

When seen on August 10, 1896, she had an extremely anemic appearance. The frontal bone showed the ravages of syphilis. Several places on the forehead were dark colored and painful on pressure (Fig. 7). She complained of excruciating pains in the bones, especially at night. There was a small opening in the hard palate leading to the nose. The bones of the nose were necrosed.

The left lung was the seat of tubercular inflammation. There was slight dulness or percussion. Auscultation revealed sibilant and crepitant and sonorous râles on the left side only. The patient at this date was too weak for a thorough examination. The treatment consisted of morphin, whisky and potassium iodid. She lingered but a few days at the hospital, and died suddenly of asthenia.

Her body had been removed before I could have an opportunity of making a post-mortem examination. She arrived at the Female Hospital, August 12, in articulo mortis, and a lethal termination was awaited every moment (Fig. 8).

Such are the condensed histories of three cases which have come under my observation. A circumstance which will be noted in these is that the two hospital patients did not fare as well as the one who was in circumstances which permitted her to resort to the care and attention of a physician. This is in no way intended as a reflection upon the hospital management, but rather to call attention to the fact that the patients in the hospitals had the disease much further advanced than the one who had not waited so long for surgical interference. Nothing could be reasonably done for Case III, as she was almost in the last stages of tuberculosis of the lungs and a morphinomaniac. Her extremely emaciated and worn-out constitution precluded all hope of betterment. Her tissues were absolutely valueless, and all the functions were defective. She had forgotten when she last menstruated, and had sunk into a condition of complete hebetude.

The condition reported in these cases is called by the name of tertiary syphilis, and yet the question which arises is, Whether it is syphilitic or not. It is observed in syphilitics and it is tertiary, it is true, in a chronologic sense of the word, but is it syphilitic? Microscopic examinations of the pus from the bones showed it to be teeming with pus micrococci and staphylococci, as also with débris of bones and connective tissue, both structural and cellular. Pity it is that we cannot yet call in the bacterium of syphilis to prove the process a purely syphilitic one. But observation, examination and experimental cultures revealed no organisms beyond those mentioned above. Following the line so ably drawn by A. Fournier, I should call these lesions parasyphilitic in the true sense of the word, and shall continue in this opinion until better reasons to the contrary and a better word to explain the condition are presented. Before a consideration of what authors have said of the condition described it may not be inappropriate to say a few words on the treatment pursued.

The primary rule of bone surgery was followed in these cases. Necrosis and caries of bone demand removal, and this was the course pursued in Cases I and II. Case III was not in a condition

fit to warrant surgical interference. There can certainly exist no doubt as to the propriety of such a course of action, and the results which were obtained is the best proof of this. The necrosed portions were not simply lifted up, but the irregular and roughened edges were made even by chiselling, thus affording a better tissue whence healing process might develop. The large openings thus left were afforded an opportunity to develop rounded and good borders, and the covering membrane was freed of the irritation to which it had been subjected by the roughened bone overlying it. This membrane thickened and toughened and became a most serviceable substitute for the bone which had been removed. It must be added, however, that there existed but little vascularity in this thickened membrane, and that, on this account, it was not deemed proper to attempt any bone grafting in the hope of producing new bone. As the result was a comparatively good one, it was deemed best to let it remain as it was. Further observations and experiments will be necessary to come to an absolute conclusion on this matter. And to arrive at a certainty the conditions should be duplicated so far as the pathologic condition present is concerned. As we have determined so far, the dura mater is efficient, becomes thickened and indurated to an extent sufficient to be serviceable under ordinary conditions. The effects of extreme heat and cold upon it have not been observed, so that nothing definite in this regard can be stated, except that the patients so situated instinctively protect the parts which have been deprived of their bony covering. Some surgeons who should know better have suggested substituting for the removed bone a silver plate or one made of aluminum, vulcanized rubber or celluloid. Of course, it is unnecessary to pay any attention to such suggestions, as they are beneath consideration.

A question of some interest is that concerning the mental state of these patients before and after operation. Before the operation patients I and II were mentally depressed and had short moments of melancholia. All hope of partial recovery even had left them, and they would not converse. After the operation they became observant and developed a more or less irritable and morose disposition. Yet, any one speaking to them in a reasonable manner would find them ready enough to engage in conversation. Neither one ever developed focal symptoms nor experienced subjective symptoms, which is sufficient evidence that the brain had not been seriously impaired. Pa-

tient III, on the other hand, was weakened by the disease process and the large quantities of opiates ingested. There was present complete hebetude, so far as taking any interest in her environments was concerned. An intense pain was present, despite the obtunding influence of the narcotic which she took. An idea of this intensity may be gained by consulting the features as depicted in Fig. 8; during life it was pitiful to behold. It seemed to be a prolonged agony, and very little or nothing could be learned of the mental condition of the woman. At her best she evidently had not been a very bright or intelligent person, and she bore the physical stigmata of a degenerate. When able to answer questions she did so in a listless manner, evincing no interest in her condition.

The subject of syphilitic necrosis of the frontal bone has occupied but little of the attention of syphilographers, but a few may be quoted here as throwing some light on the subject. Edward Lang, of Vienna; Louis Jullien, of Paris, and Charles Mauriac, of Paris, may be regarded as the best representatives of Europe so far as critical investigations of this condition are concerned. They are all agreed upon major details, and, so far as minor points are concerned, they vouchsafe but little information. One point brought out by Jullien is perhaps the best from a pathologic point of view. He states that the necrosis of the flat bones is brought about primarily by a gummy infiltration between the two tables of the bones, and this in turn causes pressure-atrophy accounting for the worm-eaten appearance of the bone when removed. Of course, in these cases gummy tumors may form on the outside of the skull, as noted in my cases, or they may be developed on the dura. In the latter case there develop symptoms of meningitis or of encephalitis, with the probabilities of such cases soon ending fatally. A strange fact which I have noted in the writings of syphilographers is that when describing the pus which forms in this variety of syphilitic necrosis they do not speak of their bacteriologic findings. In the three cases which I have seen, the cause of the necrosis was gummas situated on the outer surface of the bone, and the pus teemed with streptococci and staphylococci. The same condition has been noted in cases of necrosis of other flat bones of the skull more limited in destructive changes so far as superficial area is concerned, but as deep. We can easily account for the presence of these bacteria, which were derived from the environments of the patients. In cases in which the gum-

mas were on the meninges there are no records on this point, any more than in the other form, and, not having had an occasion to examine such, I cannot give any testimony on this point. Moreover, the pus should be obtained in such cases before it has been exposed to the air. This certainly opens up a field of investigation to workers.

Neurologists have very thoroughly studied the cerebral and mental symptoms of gummas of the brain and meninges, but they do not seem to have considered the necessity of investigating for bacteria, more especially in those cases in which the flat bones of the skull have become involved. Of course, it is not my purpose to enter into an inquiry concerning the cerebral and meningeal symptoms of gummas of the intracranial structures, nor of the various osseous changes in the interior of the skull of syphilitic origin, such as osteomas, osteophytes, etc., but rather to endeavor to establish the cause of the necrosis and of the caries which are observed. There is much yet to be done, and a more careful examination of future patients will do much to clear up this question, which seems yet to be involved in obscurity.

Rhinology

NOTES ON THE TREATMENT OF HAY FEVER AND ASTHMA

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It is not the purpose of this paper to give an exhaustive therapeutic review, but merely to call attention to certain modern ideas, or old ones revived, that are being advocated in the treatment of hay fever and asthma. It seems proper to consider these diseases together, since they are so often associated clinically. Out of 400 cases of hay fever recently reported by Thost, 266 are said to have had attacks of asthma, a proportion somewhat in excess of that occurring in my own experience.

A glance at the large volume of literature related to the subject discloses the diversity of views regarding etiology and apparently the futility of therapeutics. For example, one who believes in the ocular origin of hay fever recommends the use of smoked glasses; another, accepting the uric acid theory, saturates the system with agents intended to counteract hyperacidity and prescribes a rigorous diet; a third, regarding it as a pure neurosis, employs various so-called nervines and tonics; and, finally, the narrow view of the rhinologist demands the extirpation of all intranasal tissues thought to be anomalous and possible excitants of reflex disturbances.

As to asthma, read the list of qualifying adjectives applied to it—renal, gastric, cardiac, bronchial, and so on,—and be convinced of the confusion prevailing and of the fact that the bronchial phenomena do not constitute the essential disease, but depend in a reflex way upon some remote cause. There is hardly a more ludicrous example of false reasoning than the attempt to refer a bronchial asthma to the condition known as *hyperidrosis pedum*. This remarkable pseudo-scientific principle is established by the observation

of three cases in which the asthma ceased after the perspiration of the feet had been checked.

Rhinology has suffered a measure of disrepute in consequence of the extravagant statements of its votaries and of the wholesale sacrifice of intranasal structures, due in part to the teachings of Hack and his followers. It is equally unreasonable to deny the existence of nasal neuroses and to maintain that a "white swelling" of the knee is a nasal reflex. The concurrence of asthma and nasal polyps has been so often observed that abundant opportunity has been given to prove the occasional causative relation of the latter. Conversely, a first attack of asthma may result from removal of nasal polyps. Yet we should be constantly on our guard to discern the psychical element in cases of this class. More than once it has occurred to me to witness the disappearance of asthmatic symptoms on removal of a nasal synechia or other abnormality, only to meet with recurrence of bronchial disturbance after the lapse of a few weeks or months, the nose still remaining healthy. On the other hand, in 17 cases of recurrent asthma out of 32 "cures" reported by Schmiegelow, a return of the local nasal complaint was observed. It is interesting to note that of the cases of asthma seen by this authority 40 had chronic rhinitis and 31 had nasal polyps. In other words, of 139 cases of nasal polyps about 22 per cent., and of 514 of chronic rhinitis about 8 per cent., had asthma. Of 500 cases of asthma treated by Lublinski, 143 were known to have had some pathologic nasal condition, while it doubtless existed in a large proportion of his cases which were not specially examined. In studying 2130 cases of asthma, Brügelman, of Wiesbaden, determined that 1900 were of reflex origin. Of the latter 665 were traced to asthmagenous zones in the nasal fossæ, and 464 to similar areas in the pharynx. In a discussion on "Neuroses of the Upper Air Tract," at the last meeting of the American Laryngological Association, Makuen referred to a case in which a spasm of asthma was excited by probing a "large thickened spot of mucous membrane on the posterior wall of the pharynx." After this area had been cauterized it was found impossible to provoke an attack of asthma. Pressure from deformity or growth of some kind, inflammatory swelling or edema, and hyperesthesia are the conditions to be sought as possible causes of reflex disturbance.

It is well, therefore, in all cases of asthma to examine the nose

as well as the pharynx, and we may sometimes demonstrate the origin of the disease by mitigating or abolishing bronchial symptoms by means of an application of cocain. When no effect is observed, especially in the absence of an obvious abnormality, it is safe to assume that the upper air tract is not concerned. In any case, it is customary to combine local with general medication directed against the attack itself, as well as the underlying diathesis. Most of our patients go through what we dignify by calling "regular treatment," and in despair resort to the familiar quack nostrums in turn, many of which contain a certain proportion of well-known drugs. The relief they get from a patent medicine enclosed in circulars expounding the wonders this preparation has worked, while a physician's prescription containing similar ingredients is utterly ineffective, will remain more or less of a mystery until, perhaps, explained by Christian Science or human credulity.

It strikes one as a somewhat bold proposal to introduce a foreign body into an air tract already seriously contracted by spasm and choked with secretion, yet the intratracheal injection of menthol-glycerin and gelatin is confidently recommended by Colin Campbell. The bronchial mucosa is very tolerant, so much so that the injection of 30 grains (2 grams) of menthol and 2 ounces (60 c.c.) of glycerin at a single sitting is not considered an extreme dose. Immediate relief usually follows the first application, while several more may be needed to give permanent immunity. In the opinion of Gleitsmann, expressed in a recent paper, many, but not all, cases of asthma may be relieved by this method. His view that a cure, properly speaking, must depend upon the discovery and elimination of the cause of the disease will meet with general approval. Testimony based on a personal trial of procedures of this kind is always most valuable, and it is, therefore, interesting to hear the statement of Thomas Hubbard to the effect that he secured prompt relief of great discomfort attending a severe bronchitis by injecting into his own trachea a dram or more of medicated solution. In cases of asthma, also, he has duplicated the excellent results already reported by Anderson and others. It would appear, therefore, that tracheal injections in asthma are less formidable and more promising than on first thought might seem possible.

Atropin internally in sufficient quantity to counteract the state of nerve excitation in asthma might be thought dangerous, yet

Kremer gives $\frac{1}{16}$ grain (0.0005 gram) hypodermatically, and if necessary repeats within 24 hours, and claims good results, at the same time using other medicinal agents and dietetic measures.

The use of silver nitrate injections over the course of the vagus in the cervical region, the so-called "blocking effect" upon the heart of an electric current passed through the neck, and the internal use of adrenalin are matters requiring further investigation. As to the last, some observers pronounce it inert, while its use hypodermatically has been found effective. In this connection may be noted the remarkable experience of S. Solis-Cohen, with a local application of suprarenal extract in the form of an alarming edema of the velum, pharynx, and epiglottis. In several cases I have used it by inhalation in a 1 to 1000 oily solution without being able to determine that it had any marked effect.

The memory of the electric cautery fiasco in hay fever is still too fresh to permit unquestioning acceptance of the statements made by Alexander Francis, in his book on "Asthma in Relation to the Nose." In his most recent announcement the number of his cases of asthma has reached a total of 543, of which 316 were completely relieved, 188 were more or less relieved, in 24 results were negative, and 15 were lost to sight. The method for which these exuberant claims are made consists simply in cauterizing the nasal septum opposite the anterior end of the middle turbinate body. The treatment is based on the theory that asthma is a reflex bronchial spasm induced by disturbed stability of the respiratory center, a morbid connection existing between it and some part of the nasal apparatus without the essential coincidence of a gross nasal lesion. What he calls "disturbed stability" is referred to by others as "increased reflex irritability." A similar unstable condition of the nervous system is present in hysteria and neurasthenia. The "bronchial spasm" theory does not fully explain all the phenomena of the disease. In a recent paper by Jack, of Buffalo, attention is again drawn to the well-known fact that the bronchial tubes are encircled by cartilaginous rings which obviously must in a measure prohibit contraction of their lumen by muscular action. The asthmatic process is believed to be in addition a vasomotor neurosis, characterized by submucous edema and serous exudation analogous to the nasal condition in hay fever. By a few observers spasm of the diaphragm is assigned an important share in the causation of symp-

toms. The recent experiments of Brodie and Dixon give more or less support to this method of treatment. They found that attacks of asthma may be excited in various ways, but that most prompt and decided results follow irritation of the mucous membrane high up and well back on the nasal septum.

The foregoing views and practice are strongly upheld by Greville MacDonald, who shows 40 per cent. of cures in his cases, including polyps, septal and turbinal hypertrophies, septal spurs, as well as cases of asthma in which the septum was cauterized even in the absence of marked abnormality. To quote the words of this writer, "whatever the state of the nose, free or obstructed, with a healthy or unhealthy mucous membrane, the great majority of asthmatics are to be cured by cauterizing the upper part of the triangular cartilage." He is convinced of the genuineness of the cautery's curative power and of the absence of suggestion in his cures by the wide range of age in his cases,—14 to 70 years; without committing himself as to whether he considers youth or old age the more plastic period of life. Our thoughts go back to the time of that famous and fashionable seventeenth century physician, Dr. John Radcliffe, whose record for curing asthma is nearly equal to that of his modern rivals. The details of his method are not vouchsafed us, but he must have been the fortunate possessor of some mysterious agent no less potent and impressive than the electric cautery, since he is said to have had a marvellous reputation in the management of this dread disease. There were scoffers in those days, and in these there are some who doubt and even go so far as to intimate that the rhinologist's diagnosis of asthma is not always trustworthy. Exactly how the act of searing the Schneiderian membrane with a cautery point is to restore the equilibrium of the respiratory center no one pretends to say. If the fact that it does so is confirmed, we ought not to quibble about the *modus operandi*.

The application of this method of treatment is so easy and painless under cocain that we may expect it to be widely tested. This is to be ardently desired, even at the risk of consigning another delusion to the crowded limbo of blasted hopes.

In these days of germs and antiseptics, of organotherapy, of serumtherapy, and all the rest, it would be strange if the energy of some busy mind had not been directed along these lines in connection with hay fever. Accordingly, it appears that W. P. Dunbar, of

Hamburg, professes to have succeeded in extracting from certain grasses and cereals a toxin capable of causing hay fever in those susceptible, while it is innocuous in others. A similar idea suggested several years ago by Curtis resulted in the manufacture of a preparation of *Ambrosia artemisia*, which has been exploited with great commercial enterprise. Its alleged success furnishes additional proof of the psychical element in hay fever. By a series of animal inoculations, Dunbar has also prepared an antitoxin which allays the disturbance caused by the toxin and is said to arrest or modify the symptoms of the disease itself. Mechanical irritation by pollen or other particles has often been cited as a probable exciting cause of hay fever, but its complete absence from the toxin offered by Dunbar is conspicuous. It has been suggested that the different forms of allied vasomotor disturbance, paroxysmal sneezing, rose cold, autumnal catarrh, etc., depend each upon a different irritant, and that every individual has his own particular poisonous pollen. From this point of view it is rather discouraging to hear that Rosenfeld has added to the list of noxious pollens by discovering near Stuttgart another plant which is capable of causing typical hay fever. On the other hand, Dunbar asserts that some of his toxins are interactive, that is, a variety of antitoxin derived from one will control an attack excited by a different pollen. Results thus far reported show the discrepancies usual with a new remedy, but establish the fact that the serum is inert in those not susceptible to hay fever, and confirm the belief that in those who are, some peculiar state of nervous erethism exists which we call "predisposition." Luebbert and Prausnitz report 285 cases, about 60 per cent. of which were cured, about 30 per cent. were relieved, and in the remainder results were negative. They corroborate the view that the applications must be renewed at intervals of a few hours, since the effects are temporary, and they also call attention to the advantage of the serum in powder in that it is stable, while the fluid serum easily becomes contaminated, and is then useless or worse.

The hypodermatic use of the serum has been abandoned in consequence of the violent local reaction it excites. Mohr, who is an adherent of the pollen theory, and is himself a victim of hay fever, verifies the efficacy of the serum treatment in his own person, and in addition has devised a nostril filter whereby the sensitive membranes are protected against the invasion of irritating particles. A

combination of serum and filter ought to accomplish the final banishment of hay fever. Immerwahr, who is also a sufferer, on the other hand, has found no relief from the serum, although while using it he improved somewhat during rainy weather. Under such atmospheric conditions nearly all patients are better without any treatment whatever. Opposed experiences like the foregoing enforce the necessity of the most careful observation, lest we be led into error. Fink, who is an extreme nihilist both as to the serum treatment and the vasomotor theory of etiology, cures 95 per cent. of his cases in a few days by daily insufflating aristol into the maxillary antra. He believes that irritation of the trigeminus is the cause of the disease, and that the characteristic secretion comes from the sinus cavities. He stands almost alone in the latter contention.

My own experience with hay fever the past season is limited to 14 cases, of whom 9 used the Dunbar serum in powder. Two of these were cases of paroxysmal sneezing under treatment in the early spring, with so little result that they did not give the serum a fair trial during the hay-fever attack. Of the remainder 5 have reported decided amelioration. All my patients but one were females, ranging from 15 to 55 years of age, and all had given symptoms of hay fever for at least three years preceding. One typical case, that of a married woman, 35 years of age, who had had hay fever for ten years from the middle of August until the first cold weather, writes that she has had very little discomfort, and for the first time in years has been able to get undisturbed sleep at night. A rather curious case was that of a youth of 16 years, who spent the summer at a seaside resort on Cape Cod, who returned to his inland home the first week in September, and on the way developed hay fever which lasted three weeks. Two of my patients declare that they saw no effect from the powder except that it caused violent paroxysms of sneezing. Unlike most other therapeutic novelties, this one is not promoted with extravagant eulogies. We are cautioned not to expect too much, and over-confidence is still further averted by the earnestness with which attention to diet and hygiene is urged.

There are three drugs used more or less in hay fever which may be briefly referred to here,—cocain, adrenalin, and quinin. The first, cocain, is mentioned only to be condemned as a therapeutic agent. It should be reserved for diagnostic and operative purposes.

In most cases the very marked immediate relief it affords is followed by a stage of reaction possibly worse than the original condition. Moreover, the danger of a cocain habit is not to be ignored.

While by no means an utter failure, it must be admitted that adrenalin as a cure for hay fever has not come up to expectations. In a large proportion of cases it contracts the swollen tissues, thus relieving stenosis; it allays irritability and controls hypersecretion. Not only are these effects very transient, but in some cases they are exactly reversed. Instead of calming the irritated membranes, the application excites uncontrollable sneezing and aggravates all the distressing symptoms. Sometimes these results may be obviated by diluting 1 to 1000 adrenalin solution with normal salt solution. It has at least three advantages over cocain,—namely, it is non-toxic, it is followed by little or no reaction, and its continued use involves no danger of a drug habit. Therefore, it may be safely intrusted to the patient. Unfortunately, the early pleasing effects are not altogether maintained under prolonged use.

On the microbial theory the local use of quinin was once suggested by Helmholtz, but its success has not been brilliant, and it has been practically abandoned as worthless. So long ago as 1887, Sir Andrew Clark used quinin as one of the ingredients of a “shot-gun” solution for painting the nasal mucosa in cases of hay fever; but it is not clear how much importance he attached to this as compared with other parts of his formula, which reads as follows:

Glycerin of carbolic acid (B.P.)	1 ounce	30
Muriate of quinin	1 dram	4
Perchlorid of mercury	$\frac{1}{4}$ grain	0 015

In spite of the preliminary use of cocain the application is painful, and is often followed by considerable reaction. If necessary, it is repeated on the second to the fourth day, but never more than three applications are required. One-third of his cases (total number not given) were followed up and found to be cured for the season, while in 4 the cure was permanent. In his monograph on asthma (1894), Thorowgood mentions quinin, 1 grain (0.06 gram) in 1 ounce (30 c.c.) of water, to be used in the nose with a douche or syringe, and quite recently it has been recommended locally in hay fever by H. D. Fulton. The latter uses it in saturated solution as a spray, and follows with an ointment, 30 grains

(2 grams) to 1 ounce (30 c.c.) of vaseline, repeated every three or four hours. He claims unusual success in modifying all the unpleasant symptoms. My own experience with Clark's solution, beginning soon after the publication of his paper, has been satisfactory in a few cases in which no gross lesion could be detected. Instead of using it in the haphazard way originally proposed, it has been my custom to try to limit the application to areas shown to be especially hyperesthetic. The results with the quinin spray and ointment treatment seem to have been so pronounced and its employment so easy as to encourage further trial.

There are few pursuits more entertaining than to watch the zeal and ingenuity with which the field of a new therapeutic suggestion is widened. When paraffin prosthesis was first introduced by Gersuny it was intended as a sop to human vanity. Its use for cosmetic purposes presently extended from the face to parts supposed to be concealed from public view. Later it was used in the nose for the cure of atrophic rhinitis, and now we hear that Brindel, of Bordeaux, proposes to cure hay fever by intraturbinate injections of paraffin, with the design of compressing and clogging the secreting machinery, and thus putting a stop to the watery effusion. This practice presupposes that the mucosa of the turbinates is the sole source of the discharge, and that the rhinorrhea is the essence of hay fever, both of which assumptions are probably erroneous.

The interesting investigations by Michaels, and in this country by Braden Kyle, of chemical changes in the nasal and buccal secretions in hay fever have not attracted the notice they merit. A subacid condition of the mucus resulting from faulty elimination on the part of the emunctories is attended by an excess of ammonium salts in the physiologic secretions, which is a source of irritation and a cause of hay fever. The obvious lesson is to correct the state which leads to the formation of perverted secretion. Kyle asserts that he has demonstrated the importance of the idea in a number of cases by rapidly changing the reaction of the secretions, and that he has thus in many instances succeeded in warding off an attack.

In judging of the effect of a remedy in hay fever, one must not forget that climatic and seasonal influences vary, that is, the severity of an attack depends largely upon atmospheric conditions. Moreover, the personal equation should not be overlooked. Most of these patients are very impressionable and amenable to suggestive thera-

peutics. In order properly to test a drug or method of treatment, it is well to give no intimation of the effects expected, to observe a large number of cases, and to extend the study over several consecutive years. Thus we may hope to eliminate the influence of suggestion, to escape drawing false conclusions from insufficient observations, and to avoid being misled by the varying effects of seasonal changes.

CARBONIC ACID GAS APPLICATION IN RHINITIS

BY A. ROSE, M.D.

Of New York

THERE is a tendency at present among the medical fraternity to take up the study of the history of medicine, a study which for a while, over the many new theories and discoveries, had been sadly neglected.

John Kanold, in the year 1708, wrote: "It is to be hoped that at this time no one who has common sense will deny that the *historia morborum* is the most important and most valued support of the whole of medicine, because, by thorough knowledge of this history, we learn to arrive at the true pathologico-etilogic conception and consequently we find the necessary and reliable *indicationes curativæ*."

And what he said is true to-day. A few dates as introduction to the subject under consideration will furnish evidence how much we can learn for every-day practical use from the physicians of past centuries. We shall see that some of their methods and remedies surpass many of modern date.

The history of the discovery, first demonstration, and description of carbonic acid gas are hardly mentioned in the text-books; and of its therapeutical application in olden times almost nothing can be found in the literature of the present day.

The modern writers confine themselves to the stone of Memphis, which was dissolved in vinegar and applied to parts of the body in order to produce anesthesia; they also mention something about Paracelsus (1493-1541), that he knew the gas produced by burning charcoal was identical with that developed when limestone was heated to a high degree; but of the next man who plays an important rôle in the history of carbonic acid, of Jan Baptist van Helmont (1577-1644), one of the greatest chemists who preceded Lavoisier, of van Helmont, the founder of pneumatic chemistry, some of us may have heard very little.

He was the first who used the word gas as a generic name for all

elastic aëriform fluids, in order to distinguish them from atmospheric air. He paid much attention to the study of gases, showed that they entered into the composition of the atmospheric air, he was the first who gave a description of carbonic acid, which he called *gas sylvestre*. He demonstrated its development when acid is brought in contact with limestone or potassium, at wine and beer fermentation during putrefaction, its appearance in the stomach, showed that it was contained in the mineral water of Spa, that it was rising from the ground in some places, for instance, in the dogs' grotto near Naples.

It may be of interest to mention that he was one of the men with new ideas who had to combat with misocainia; he was imprisoned for two years for having spoken against Christian Science, that is, against the healing power of religion; he was called all sorts of names because he did not believe in blood-letting as a remedy against all kinds of diseases, and in a necrology it was said that he never had accomplished anything of value.

Robert Boyle (1627-1691) confirmed the discoveries of Paracelsus and of van Helmont, showed how to separate and to handle the gases, but he was not aware that carbonic acid and hydrogen were essentially different gases.

Frederick Hoffmann (1660-1742), who was in correspondence with Robert Boyle, discovered some qualities of the gas contained in mineral springs, and called it *spiritus mineralis*. Observing that when in watery solution it would color vegetable matters red, he judged that it was a feeble acid.

Joseph Black (1728-1799) was another great promoter of the science of chemistry. His important experiments with carbonic acid demonstrated its combinations with alkalies. He assumed that it existed in solid form in alkalies and called it fixed air; he also supposed that it was produced by the act of respiration, proved that it is absorbed by caustic alkalies and disengaged again under effervescence when acid is made to act on the combination.

Lavoisier (1743-1794), among the sons of his country the greatest, the most perfect man of science, died on the guillotine, a victim of the French Revolution, discovered the chemical constitutions of carbonic acid, that oxygen and carbon were its constituents.

In 1823 Faraday succeeded in liquefying, and in 1835 Thilorien in solidifying, carbonic acid gas.

Hey (1736–1819), Withering (1741–1799), Dobson Warren (1753–1815), Macbride (1726–1778), Ingenhouse (1730–1799), Beddoes (1760–1808), Henry (1755–1836); Rotheram (died 1787), and White were the first to make systematic use of carbonic acid gas for therapeutic purposes. Macbride applied it to scorbutic ulcerations, Percival, as a palliative measure in phthisis; he was aware that it could not be considered a radical remedy. If Bergeon had studied the writings of Percival he would have saved us a deception about twenty years ago.

Priestley (1733–1804), the friend of Benjamin Franklin, whilst at Leeds, lived near a brewery; it was this circumstance that first directed his attention to chemical matters. He had read of fixed air, and, being desirous of making himself acquainted with its properties, he took advantage of the fermentation process to procure some. Priestley at this time had little or no knowledge of chemistry, he was possessed of no apparatus, and had scarcely the money to procure any. But these very circumstances were the sources of his success, since he was under the necessity of devising original processes and appliances suited to his narrow means and peculiar views. If, he says, I had been previously accustomed to the usual chemical processes, I should not have so easily thought of any other, and without new modes of operation I should hardly have discovered anything materially new. Priestley made his discoveries with a very imperfect apparatus and without general knowledge of chemistry. Notwithstanding all this, chemistry is indebted to him for the most important instruments for studying the gases.

It is tempting to speak more of this most remarkable man, but his wonderful history is familiar to us, and under these circumstances the attempt to do him justice would require a whole book. He recommended the application of the carbonic acid gas-bath in fevers and septic conditions, and also as a palliative measure in case of cancerous ulcers.

The methods of generating and applying the gas as practised by the physicians of the eighteenth century were, naturally enough, rather primitive ones. The part of the body to be acted upon was brought over the opening of a vessel in which carbonic acid was developed. Sometimes a bladder was filled with the gas, and from this bladder the gas applied to the parts to be treated.

As mentioned before, Percival and Macbride treated scorbutic

ulcerations with carbonic acid. White, the author of a book on midwifery, recommends topical application of the gas in croup, as also did Henry, Dobson, Percival, Warren, Lee, Rotheram, and other physicians of the same period. Dobson made use of the gas douche successfully in phagedenic ulcers. The same physician praises its good effect in variola. He placed children suffering from this disease naked over an effervescing mixture of tartaric acid and bicarbonate of sodium, or he directed the gas douche upon the different regions of the body. Especially interesting for us is the fact that Percival treated ozena by topical application of carbonic acid gas; he brought it in contact with the nasal cavities through tubes, and speaks of this remedy as the best means to cure the offensive odor of ozena. Many physicians of the eighteenth century have employed and recommended it in the treatment of ozena, but with one exception, which shall be mentioned presently, in our literature of the present time, at least in the writings of the specialists on diseases of the nose, carbonic acid is not even mentioned. The last advocate of whom I found a record was Demarquay, who over fifty years ago said that the carbonic acid gas douches modify and promptly cure the morbid discharges of the Schneiderian membrane.

While during the eighteenth century external application of carbonic acid for therapeutic purposes was so extensively in use in England, French physicians likewise directed their attention to this remedy. In 1777 Champeaux, a surgeon of Lyons, won the prize of the Academy of Surgeons of Paris for an essay in which he treated of the external application of carbonic acid gas in different forms of ulcer. There appeared other publications on this subject in France at that time—one by Rozier, in 1776; another by de La-louette, in 1778; the title of the latter is "*Resultat des experiences, faites sur les propriétés de l'air fixé, appliqué au traitement de plusieurs maladies externes et chirurgicales.*"

The history of carbonic acid gas in therapeutics, especially in the form of dry gas baths during the nineteenth century, is very important, but, except in the writings of Demarquay, I did not find records of new observations of its employment in rhinitic affections, and, wishing to concentrate the attention to this particular subject, I shall reserve the further history of carbonic acid treatment in general for some other occasion.

Dr. Joal, a French physician of Mont Dore, has quite recently

reported his observations on the effect of the gas in rhinitis. He found that the gas acted as a vasoconstrictor, as an anesthetic, and as an antiseptic. He describes the effect as follows: When the gas is brought in contact with the nasal mucous membrane it produced at first a prickling but quite tolerable sensation, followed by an agreeable, refreshing effect of warmth and dryness. The examination of the mucous membrane shows reduced sensibility to such an extent that otherwise painful cauterizations and explorations will cause no pain; then follows excitation of the nerve-ends, producing vasomotoric dilatation and glandular hypersecretion; after this nervous activity becomes exhausted, the vessels become constricted, and again anesthesia will be noted.

The best results were observed by Joal in the treatment of hyperesthetic rhinitis, especially in that form which characterizes hay fever.

In case the application of the gas does not cure completely vasomotoric coryza, it will at least ameliorate to a marked degree the inflammatory symptoms.

Dr. Joal believes that the employment of carbonic acid gas is indicated to combat the microbic element of hay fever; he believes in the antiseptic effect of carbonic acid in these instances. I have not been able to see the original of his report; in the abstract from which I quote, nothing is said upon which facts Dr. Joal bases his theory. All I know is:

As an antiseptic it is of limited value. When antiseptic principles were first established in the treatment of wounds, all wound remedies were tried as to their germicidal powers. In regard to carbonic acid we know now that certain bacteria can live and thrive in it almost as well as in atmospheric air; that others develop imperfectly or slowly, and that a third class grows in it only when the cultures are exposed to breeding temperature. Saprophytes, although they do not thrive in it, do not perish in carbonic acid. It does not affect the bacillus of typhoid fever, but it destroys the bacteria of anthrax and cholera. It interested me very much to learn from Dr. Alice Byram Condict, of Bombay, India, one of the matriculates of the New York Post-Graduate Medical School, while I was lecturing on carbonic acid before the class, that the physicians in India—the home of cholera—insist strictly that people should drink no other water but that charged with carbonic acid.

Carbonic acid gas is to be considered as a remedy of the first order in the initial stage of an ordinary rhinitis, but in all forms of rhinitis as a means to ameliorate the intensity of the symptoms.

Physicians of the eighteenth century have claimed that certain cases of anosmia can be cured by means of carbonic acid gas application, and the same assertion is made by Dr. Joal.

In none of the writings on carbonic acid gas application in rhinitis have I found anything on the gratifying effect in cases of children, even infants. I consider my own observations in such cases of especial value. In naso-pharyngeal diphtheria it surpasses by far the methods of irrigation or syringing, which are so disagreeable and even dangerous. While children will struggle against this procedure, and threaten them, they rather enjoy the gas treatment; they ask for it after they have once experienced its gratifying effect. The nose becomes disengaged from the accumulated mucous or purulent matter, the little patients are able to breathe freely through the nose, and can keep the mouth closed even during sleep. They are anxious to apply the nozzle themselves as soon as they feel the necessity of relief.

A curious observation which will prove of importance if confirmed in more instances is this: I found that patients once treated for some length of time with nasal carbonic acid gas douches would be less vulnerable in regard to the Schneiderian membrane. They would be free from the accustomed rhinitis during the cold season.

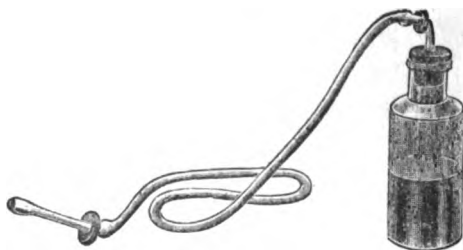


FIG. 1.—Simple apparatus for carbonic acid gas applications.

The first apparatus which did me good service and which has the advantage over the others that it can be easily improvised, as a rule, with the aid of a nearby druggist, consists of a bottle, holding a pint or a little less, with a wide neck and a rubber stopper perforated so as to admit a tube, with a nozzle, as the case may be, for nose, rectum, or vagina (Fig. 1). A solution of 6 drams (24 grams)



FIG. 2.—Cylinder for making carbonic acid gas applications.

of sodium bicarbonate in 6 to 8 ounces (180 to 250 c.c.) of cold water is introduced into the bottle, and 4 drams (16 grams) of *crystallized* tartaric acid (if pulverized acid is used, the development of the gas goes on too rapidly) is added. The larger these crystals are the better. Instead of the tartaric acid crystals, disks of acid sulphate of sodium may be used. The bottle is then closed, and the carbonic acid developing in the water rises through the tube, the nozzle of which has been placed in position. This form of gas generator serves quite well to apply the gas to the nasal cavities, to inflate the rectum, and in some instances it can be used to give vaginal douches. Gas develops during about 10 to 12 minutes. Its disadvantage is that the current of gas can neither be regulated nor interrupted.

A much better apparatus, especially convenient for office practice, is the one represented in Fig. 2, consisting of a gas cylinder containing about $2\frac{1}{2}$ pounds of liquid carbonic acid. The gas current, passing through a tube attached to the cylinder, can be regulated to a fine point and its strength watched with accuracy when a wash-bottle is connected with the tube, as shown in the cut.

The only precaution, besides regulating the current, is to see that the patient keeps the mouth open while the gas passes through the nose.

Ophthalmology

MAJOR TRAUMA OF THE EYE IN GENERAL PRACTICE¹

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IN every industrial community injuries to the eye are frequent, and so disastrous in their effects may they be, at times, affecting not only the producing power of the person injured, but often the very sustenance of many dependents, that their treatment constitutes one of the most important and responsible branches of surgery. The conduct of the case immediately following injury, and during the succeeding few hours, often determines the final result. The tissues of the eyeball, all of them highly specialized, are prompt to resent inflammatory excitants, and, unlike tissues in other parts of the body, are not well substituted by connective tissue, which is the inevitable product of destructive inflammation. The two great objections to newly-formed connective tissue are (1) that it contracts, and in doing so in the eye may not only distort, but totally destroy, the usefulness of the organ; and (2) that it is not transparent, and, if occupying the line of vision, it causes permanent damage.

The primary indications, then, in the treatment of all injuries to the eye are to prevent inflammation, and to preserve function. Inflammation, once established, must be combated with the ever-present purpose of maintaining throughout, and ultimately, so far as possible, function intact. Of little use is an eye which has passed through a severe attack of iritis, and has finally emerged from the fray with the iris forever bound to the lens capsule, and the pupil filled with dense and unyielding exudate. Such an eye cannot see,

¹ Read before the Burlington County (N. J.) Medical Society, June 14, 1905.

and operative procedures at a subsequent time are, as a rule, unsatisfactory.

When called upon to treat an injured eye, therefore, it becomes our duty to see well into the future, and to remember that, however well the eye may look when we are through with it, it is entitled to do some of the looking.

As major traumas of the eye, I will consider some only of those more common injuries which imminently threaten vision, directly or indirectly, and, although injuries to the lids may ultimately damage or destroy sight, I will confine myself mostly to the eyeball, which is the true visual organ.

Ocular traumatisms may be divided into those due to chemical agencies and those due to mechanical agencies; and wounds of the eyeball due to mechanical agencies may again be divided into non-perforating and perforating. The latter differentiation is a most important one, for the moment we have perforation of the eyeball, that eyeball becomes at once exposed to all the dangers of infection, and the gravity of the case is many times increased. Before considering these various forms of injury, it might be well to call your attention briefly to the general symptoms of ocular injury, at the time of its infliction. They are doubtless well known to you, and are practically the same, no matter what the variety.

So important is the organ of vision that nature has provided it with protective surroundings, ever ready to aid and assist from the moment of attack. It requires but slight irritation to cause a spasmodic contraction of the orbicularis palpebrarum muscle and a copious flow of lacrymal secretion. Thus it is that an injured eye is invariably closed, and resists attempts at opening, and when opened the conjunctival sac is found filled with tears. Furthermore, when opened, the eyeball will be found to be rotated far upward, the cornea seeking, so far as possible, protection under the upper lid. With the blepharospasm, the extreme sensitiveness to exposure, and the upward rotation, examination is difficult. And right here let it be understood that complete examination is necessary for diagnosis, and must be made. Never take for granted what has not been seen, rather than make a distasteful investigation. By the exercise of a little patience, and attention to the methods to be employed, almost any eye can be sufficiently examined. In a good light, with the fingers of one hand resting on the forehead,

place the thumb near the margin of the upper lid. The thumb or a finger of the other hand is placed against the lower lid. The moment the lids are touched and an effort is made to separate them, the orbicularis spasm is increased. This is the time for patience and judgment, and, instead of attempting to force the lids when the spasm is greatest, wait, exercising firm but moderate pressure, one minute, or two minutes, and the spasm will relax; the lids will gradually separate. The pressure should not be against the eyeball, but directed upward toward the orbital margin. The same holds good for the upturned eyeball. If one waits long enough, it will come down, and the cornea can be inspected. The procedure may be facilitated by the use of a few drops of cocain solution. The extent of damage can, in a general way, be determined by this preliminary inspection; but for a more critical examination it is necessary to use focal illumination, by the aid of which more minute changes in the cornea, and those in the anterior chamber, iris, and lens, can be well seen. So useful, and so simple in its application, is focal illumination, that every practitioner of medicine should carry with him at all times a condenser, which is nothing but a double convex lens of 5 or 6 cm. focal distance. By it light is brought to a focus, or concentrated upon the object under observation, and its advantages well repay the surgeon for the very slight amount of practice necessary in learning to use it. A certain amount of skill and practice is, of course, necessary to enable one to manipulate the eye with one hand and the illumination with the other, but what medical or surgical procedure does not require skill and practice?

Having made the preliminary examination, we will now pass to a consideration of the different kinds of ocular injury, their individual peculiarities, and their treatment.

INJURIES DUE TO CHEMICAL AGENCIES. — The most usual traumatisms under this heading are those due to lime, unslacked and slacked, strong acids, such as nitric and sulphuric, and alkalies, such as caustic soda, caustic potash, and ammonia. These agents are in constant use, both commercially and domestically, and are most destructive to organic tissue. Their action, if in any concentration, is rapidly escharotic, and the damage done by them both primarily and secondarily is frequently irreparable. The symptoms produced by such violent irritants as these are practically the same

for each. They cause at once pain, blepharospasm, intense lacrymation, chemosis or swelling of the conjunctiva, devitalization, and necrosis of the parts with which the agents have come in contact. Often a stringy, adherent pseudomembrane is rapidly formed upon the conjunctiva. Devitalization is characterized by a haziness or whitening of the burned areas, and, if affecting the cornea, is a most grave sign.

Secondarily, the symptoms are, as might be expected, a throwing off of dead tissue, sloughs, copious secretion (non-purulent or purulent), iritis, iridocyclitis, and, if the injury has been severe enough, general suppuration or panophthalmitis. The prognosis depends largely upon the depth of the burn. As is well known, epithelium regenerates rapidly and perfectly, and if the injury has not gone beyond this layer a good recovery can be expected. If, on the other hand, the substantia propria has been invaded, the prognosis is less favorable, and especially so if the cornea is involved, for dense scars or leukomata are sure to remain, and if in the line of vision the eye will remain forever damaged. Escharotic destruction of the conjunctiva is followed by adhesions. Such adhesion, known as symblepharon, obliterates more or less completely the conjunctival sac, prevents free movement of the eyeball, and starts a morbid cycle always distressing and difficult or impossible to relieve.

Treatment.—The indications are to remove at once all traces of the offending substance, to relieve, so far as possible, and without causing further damage, the patient's suffering, and to aid nature, herself a most experienced ophthalmic surgeon.

Unslacked lime is furious in its action, for, from contact with the tears which are pouring out from the instant it touches the eye, it at once commences to slack and generate heat. On the cornea, even in the smallest quantity, it is fatal. Authorities, and good ones, for years past, and up to the present day, in view of the affinity between unslacked lime and water, have been strong in their teaching not to douche a lime-burned eye. Oil is recommended, after which a concentrated solution of sugar is instilled, which forms with the lime an insoluble compound. But when it is considered that the eye is already filled with water, coming in a constant stream, and in sufficient quantity to dissolve all the lime at hand, and that the chemical change of slacking is a very rapid one, I am of the opinion that the first step in treatment should be a rapid, free, and more

or less forceful flushing of the entire conjunctival sac with water from the nearest source. If the lime is thus dissolved, and it is, it is likewise immeasurably diluted; all particles not too firmly adherent are flushed out, which means the greater quantity. A delay of one minute or less in getting oil or dissolving sugar might be quite sufficient to destroy the eye. After the eye is flushed, and energetically flushed, oil or sugar solution should be dropped into the conjunctival sac, but continue the flushing until these remedies are ready for use.

The same principles apply to the acids and alkalies. I believe it is better to dilute them by flushing until they are inert than to render them so by neutralization, and thus waste time hunting for and preparing the neutralizing agent. It is a question of practice against theory, and you can take your choice. This constitutes what might be called the first aid to the chemically injured eye, and we have now to combat a traumatic inflammation, the virulence of which only time will tell. Here again the indications are clear enough,—deplete and limit exudation.

Following general surgical principles, administer a purgative, and apply ice, but the latter must only be used with judgment, and its use is restricted by very important contraindications. Much harm is often done by the injudicious use of ice. Therapeutically, the action of cold is to contract the blood-vessels, and to keep blood out of the part, and limit or prevent exudation. But be it remembered, that the one structure above all others in the injured eyeball which we are endeavoring to save, the cornea, is itself without blood-vessels, and must depend upon a mesh of vascular loops at the limbus for its nutrition, which it gets by imbibition. The cornea is therefore easily devitalized, and if lusterless, hazy, and opaque, the signs at this time of devitalization, ice does little more than rob it of its only chance of regeneration. As a rule, ice is of greatest service for the first 24 to 48 hours, and must never be used when the cornea is hazy and in need of blood. Furthermore, if unsuccessful in preventing exudation, and if, in spite of its use, there is exudation in considerable quantity, that exudation must be absorbed. Stop the use of cold, and commence at once the application of heat, in the form of wet hot compresses properly administered.

Drugs.—Nothing need be said about cleansing lotions; they are always in order whenever needed. Atropin, or a similar cyclo-

plegic has an important use. It puts the ciliary body at rest, relieves the congestion of the ciliary vessels, helps allay pain, dilates the pupil, drives the blood out of the iris, prevents in many cases secondary iritis, and if inevitable, places the iris in the best possible condition for such an attack, and guards effectually against the formation of posterior synechia. One or two drops of a 1 per cent. solution of atropin used 3 or 4 times daily, if properly instilled, is a sufficient dosage.

Within two or three years, a very valuable drug has come into use, known as dionin. It is remarkable in its action, and for certain indications would seem to be almost ideal.

Dionin is a morphin derivative; chemically, it is the hydrochlorid of ethyl-morphin. It occurs as a white crystalline powder, easily soluble in water, one hundred parts of which at ordinary temperature will dissolve fourteen parts of dionin. It is a profound analgesic, affecting the deeper tissue of the eye, and is most remarkable for its vaso-dilator properties. The capillaries under its influence become three or four times larger than usual, and the lymphatic vessels become increased tenfold. It is also antiseptic, resorbent, and phagocytic. It is used in a 4 or 5 per cent. solution, and is strongly indicated in those conditions in which the life of the cornea is threatened. An eye, for example, which has been injured by ammonia, one of the most dangerous substances which can enter the eye, has perhaps the best chance for recovery with useful vision, if dionin is used to dilate the surrounding blood-vessels and lymphatics, and counteract the almost inevitable necrosis of the cornea. Ammonia accidents are, moreover, becoming quite frequent, owing to the extensive use of this chemical in manufacturing establishments, in refrigerating plants, etc., which are constantly exploding. I recently saw both eyes destroyed from the explosion of a bottle of aqua ammonia which a lady was holding under the hot water spigot, to loosen a tight stopper. In using dionin it is well to remember, that on account of the great vascular dilatation produced, the reaction is often, though harmless, apparently very severe. A few minutes after instillation of a 4 per cent. solution the conjunctiva becomes intensely swollen and chemotic, even overriding the cornea.

INJURIES CAUSED BY MECHANICAL AGENCIES.—As stated above, these may be non-penetrating and penetrating. Non-pene-

trating mechanical traumatisms are as a rule less serious than those resulting in rupture or penetration of the eyeball. The dangerous element of intraocular sepsis, at least, does not enter the equation. Aside from this, however, they can be and frequently are just as disastrous, or even more so in their effects upon vision than penetrating wounds.

An eyeball which has been struck a forcible blow, but not ruptured, presents externally a rather characteristic appearance. The lids are usually swollen and discolored (black eye); the conjunctival vessels are ruptured, causing more or less extensive ecchymosis, which, although often formidable in appearance, is really of little consequence; the pupil is often about one-half dilated, elliptical, and fixed; there may be blood in the anterior chamber, which is easily recognized by focal illumination; its presence indicates rupture of some of the finer vessels of the iris, usually near its ciliary attachment; the lens may be partially or totally dislocated. If dislocated forward it can be seen in the anterior chamber. The pupillary margin of the iris rests upon the anterior lens capsule, and when there has been a break in the suspensory ligament of the lens, with partial or complete dislocation, the iris is seen to be tremulous. Tremulous iris, or, as it is called, iridodonesis, always indicates that the lens is not in its proper position, and properly supported. Other changes are rupture of the iris either at its pupillary border or at its ciliary attachment, vitreous hemorrhage, and rupture of the choroid.

If immediately after a severe contusion of the eyeball, vision is completely lost, and the anterior visible media are reasonably clear, it is probable that there has been a large vitreous hemorrhage, and perhaps rupture of the choroid, conditions which seriously influence the prognosis.

Incised and lacerated wounds of the conjunctiva and sclera, abrasion of the cornea, etc., occur in countless variety. They present nothing of unusual importance which need be mentioned here.

Explosion of gunpowder, dynamite, etc., is a frequent cause of ocular injury. Fourth of July accidents are of this character. The lesion may be a simple burning of the lids and bulbar tissues, with impaction of powder, sand, etc., rupture of the eyeball, or complete destruction. Particles of burnt powder, sand, dirt, etc., are ground into the tissues, and cause much disfigurement. Reac-

tion is usually severe, but these cases generally do well under careful treatment. Burnt powder embedded in the cornea appears as large or small irregular dark spots. It has lost its hard granular character, and seems to be in the form of a homogeneous paste. This makes it difficult to remove, and as it stains the surrounding tissues, it is no easy matter to determine when it is all removed. The spots are to be scraped with a spud, and the spud wiped on a piece of wet cotton. When no more brown material can be scraped off, it is better to discontinue such manipulation. Cocain is a sufficient anesthetic. Powder stains, except when they are in the cornea, and obstruct vision, are harmless, but disfiguring. From the lids, forehead, and face they must be picked out, and the parts must be frequently scrubbed with soap and water. Hydrogen peroxid is said to dissolve them.

Accidents which are fortunately more rarely met with, are dislocation of the eyeball, and avulsion, or a complete gouging out of the eyeball. They are usually caused by the entrance into the orbit of some blunt instrument, such as a stick. Dislocation of the eyeball is characterized by a marked protrusion forward, and a closing of the lids behind the globe. The optic nerve and muscular attachments are not severed.

Sticks, umbrella ferrules, canes, etc., are sometimes thrust into the orbit, causing great damage, with or without injury to the eyeball. Hemorrhage deep in the orbit under these circumstances causes marked proptosis, and the lids become tense and swollen.

Treatment.—Lacerations of the conjunctiva, if sufficient in extent, are to be closed with stitches, and the eye treated upon general aseptic surgical principles. If any of the external ocular muscles are torn or divided, which is sometimes the case, they must be repaired. A dislocated eyeball must be reduced. This is best accomplished by a small spatula and a piece of greased lint. If the constriction of the lids behind the globe is too tight, divide the lid at the outer canthus with scissors, replace them in front of the eyeball, repair the canthoplasty with stitches, and use ice and compression. Avulsion calls for general surgical repair work. General anesthesia is, of course, necessary for these more extensive injuries.

In the treatment of the more common contused wounds, ice is to be used immediately, but with the same restrictions as above noted. Its purpose is to ward off inflammation; it will not aid in

the absorption of hemorrhage, therefore change for heat after 24 to 48 hours. Atropin has the same indications as in the other ocular injuries, and after the acute stage of traumatism is past, dionin can be used as an absorbent.

PENETRATING WOUNDS OF THE EYEBALL.—With these there is a triple danger. First, there is the danger of injury, *per se*; second, the danger of septic material entering the eyeball; and third, the danger of foreign bodies remaining within the eyeball. The wound of penetration may be a small puncture, difficult and sometimes impossible to find, or it may be a large rent or incision, through which the intraocular contents protrude or escape.

The clinical picture of a perforated eyeball varies with the position and extent of the perforation. If in the anterior segment involving the cornea or the corneo-scleral margin, there is at once an escape of aqueous humor, and a pushing forward of the lens and iris. The iris is frequently prolapsed, and appears as a dark mass of soft tissue extruding from the wound. The eyeball is soft. If the lens has been injured it is opaque (traumatic cataract). The bottom of a wound in the ciliary region, if of any size, is dark in color from the protruding uvea.

If the wound opens up the vitreous chamber, there is escape of vitreous humor. This may occur in any quantity from a few drops to the greater part of it. The greater the loss of intraocular fluids, the softer and less rounded is the eyeball. If there has been considerable loss the eyeball is collapsed.

From 45 to 56 per cent. of general ocular traumatisms are foreign body injuries. A small splinter of iron, steel, glass, stone, etc., penetrates the outer tunics of the eyeball and lodges somewhere within. Blacksmiths, foundry workers, locomotive engineers, etc., are frequently the victims of such accidents. Locomotive engineers and firemen are constantly in danger from the explosion of the water-gauge or oil-gauge. There is no way to prevent this except to have the gauges encased in metal, which is now done on some railroads only. A foreign body within the eye is a constant menace to that eye, and, should sympathetic trouble set in, to both eyes. All such cases should be examined by an x-ray expert. Metal and stone can be accurately located, but, unfortunately, glass cannot be detected by the x-ray.

The tolerance of the eye to foreign bodies which are aseptic

varies greatly with the nature of the foreign body. Gold, platinum, silver, glass, and graphite have been found to be chemically indifferent. Iron and copper, on the other hand, are not chemically indifferent. Copper is especially dangerous, as it is apt to cause suppuration when it comes in contact with vascular structures. The condition of the entering body, whether septic or aseptic, is of great moment in forming a prognosis. In a general way pieces of hot metal which fly off while forging, etc., are apt to be aseptic.

Treatment.—A physician in general practice should hardly be called upon to assume the responsibility of a ruptured or penetrated eyeball, which may or may not contain a foreign body, and which may or may not survive, and be a useful organ. The question of whether it is safer to attempt to save the eyeball, or to consider it lost, and enucleate it, is one which can be decided only after taking into account very many contingent factors. Foreign body injuries to the eye constitute in themselves a very large chapter, and I should advise the general practitioner to steer clear. What can be done by him, is to render the field as sterile as possible, to manipulate no further than necessary for a provisional diagnosis, and to put the patient at complete rest.

GONORRHEA AND CONJUNCTIVITIS

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At the outset we may say plainly that gonorrhea is productive of conjunctivitis under three different conditions: (1) There is the well-known acute inflammation of the eyes of the new-born child associated with the presence of a purulent vaginitis in the mother; (2) there is the violent and virulent purulent conjunctivitis of the adult whose conjunctiva has been contaminated with pus from a previous gonorrheal urethritis or vaginitis, or from a previous conjunctivitis; and (3) there is the form of conjunctivitis called metastatic occurring in a person actually suffering from gonorrhea, but in whom direct contamination does not appear to have occurred. The first two of these, being already well-recognized conditions, we shall dismiss with a few words.

Ophthalmia neonatorum, or acute conjunctivitis of infants, is a disease only too familiar both to the ophthalmic surgeon and to the obstetrician. It varies in its frequency in different countries and in different cities, and its terrible results are more in evidence in one place than in another. For example, in Edinburgh one does not, I think, meet with the condition so frequently by any means as seems to be the case in certain other towns in Great Britain. I should like to be able to attribute this relative immunity which Scotland enjoys to superiority in morals, but that certainly is not the explanation. I have always been inclined to attribute it rather to the presence of a large medical school, in the teaching of which the vital importance of care in the early recognition and treatment of such conditions has for a very long time been an important feature. Comparatively only a very small proportion even of the poorest women in Edinburgh are attended in labor by unskilled persons; well-instructed advanced students, working in connection with various medical charities and organizations, are the usual attendants, and they are awake to the necessity for immediate and vigorous measures and to the value of them. The

medical school is large, and the proportion of the extremely poor amid the population of Edinburgh very small, so that the number of cases untreated except by the favorite household remedy, breast milk, is small also, and becoming smaller. This disease at one time was the cause, as every one knows, of an enormous amount of blindness, more especially since it practically always affects both eyes, and statistics of various countries taken a number of years ago showed an appallingly high proportion of such cases; but now in all the clinics so much care is taken, so many students have the matter carefully brought before them, that gradually the leaven is beginning to "work," and we may expect still further diminution of these numbers, which, it must be confessed, are capable of very great improvement even yet. I do not propose to enter at all upon the question of the best treatment of cases of ophthalmia neonatorum, but should like simply to point to the value of certain recent additions to our available silver compounds as lotions, to say nothing of that sheet-anchor in purulent conjunctivitis, the older fashioned but still (in my opinion) unrivalled nitrate of silver. Among the newer compounds I am inclined to give a very high place to protargol. It is, of course, strictly speaking, a little beside the question, but an important practical matter in this connection is that it must not be supposed that in every case of ophthalmia neonatorum gonorrhea is the only possible cause, for cases occur from time to time in which the gonococcus is not present, and the conjunctivitis appears to be caused by other organisms, notably the pneumococcus. Knowledge of this fact has enabled me to be of some service in the pacification of a serious quarrel in the family of a patient whose morals had, on the strength of the occurrence of acute conjunctivitis in an infant, been made the subject of adverse criticism.

Acute gonorrheal conjunctivitis of the adult, caused by direct contagion with gonorrheal pus, or with pus from another similarly affected eye, is fortunately a somewhat rare disease, for it seldom passes away without leaving serious defect of sight, and very often indeed it destroys one eye, if not both. When one considers the frequency of gonorrhea and the carelessness of so many men on the one hand, and the rarity of gonorrheal conjunctivitis on the other, one cannot fail to be impressed with the idea that the normal conjunctiva must oppose vigorous resistance to the implantation

of organisms. This has indeed been shown, by Valude and others, to be the case in connection with the supposed antiseptic action of the lacrymal secretion.

For the purpose of ready contrast with certain of the peculiar features of the variety of conjunctivitis of which we are about to speak, it will be convenient here to mention briefly the chief clinical points in connection with purulent conjunctivitis by direct infection. It occurs then most usually in one eye first (for obvious reasons generally the right eye), which itself then infects the second. It may come on at any stage in the history of a gonorrhea, and is not in any way related to changes in the severity of the process which is going on in the urethra. The attack is acute, nay, violent; the pain, the swelling of the lids, the chemosis, are very severe indeed; the secretion, thin and watery for a couple of days or thereabouts, rapidly becomes purulent, and great quantities are poured out; this pus contains myriads of gonococci. Rarely, indeed, does the patient escape without the formation of an ulcer of one or other cornea, which may result in complete destruction of that structure and consequent loss of all vision. Except in association with the ulcer iritis is not frequent, and, though cases occur now and then in which some of the joints are simultaneously attacked, that is a very rare occurrence indeed. The attack in the eye is long continued and violent, but exhibits no tendency to recur once it has passed off. I have never heard of any case in which a patient has twice been attacked by gonorrheal conjunctivitis.

Regarding the third form in which gonorrhea affects the conjunctiva comparatively little has been written, so little, indeed, that several of the best text-books on ophthalmology do not even so much as mention its occurrence. A brief description of its principal features will serve to show clearly how different its clinical features are from those of the other form. We shall take the points in the same order as in the case of the last-mentioned variety. It is apt to affect both eyes at once, and even when one eye has been affected a day or two earlier than the other there is nothing to suggest that one has been infected from the other. It generally comes on during the acute stage, or during a recrudescence of the urethral mischief. The attack may be reasonably acute, but certainly cannot be described as violent, and the chemosis and swelling of the lids are simply *nil*. The secretion is mostly lacrymal,

mixed, at any rate, after a day or two, with the mucopurulent secretion of a slight conjunctivitis; there is no pus whatever, nothing worse than muco-pus, and this contains no gonococci. Ulceration of the cornea, as well as iritis, is not an infrequent symptom, but this is in the form of small superficial ulcerations which hardly can be said to spread at all, and which heal without any visible scar. As regards the precise significance of these there is not much that requires to be said, for they do not leave any permanent result, and as a matter of fact it is probable that these ulcers are due to the presence of adventitious organisms. Iritis of a more or less plastic type seems to be far from infrequent, and the joints are often affected at or about the same time. The attacks in the eye are of short duration, but are exceedingly apt to recur. From a comparison of the statements thus made regarding conjunctivitis by direct infection and by metastasis it becomes plain that the two conditions are essentially distinct.

The notes of two cases may help to emphasize this.

CASE I was that of a young chemist whom I was asked to see. Three months previously he had acquired gonorrhea; under judicious treatment he had recovered almost completely, but about three weeks before my interview with him the urethra had again begun to secrete pus without any apparent additional reason; at the same time he complained of pain and swelling in several joints, and conjunctivitis had come on. Under treatment by his own physician these symptoms had passed off, only to recur; and I was then consulted. I found him to have a moderate degree of conjunctivitis, resembling in its degree of severity a fairly acute Koch-Weeks conjunctivitis, but not even approaching that of the ordinary gonorrheal. The membrane was moderately injected, there was a good deal of watery secretion mixed with muco-pus; there was some hyperemia of the iris, but no real iritis. Under treatment with protargol and corrosive sublimate lotions he recovered quickly and left Edinburgh. I regret that the circumstances in which I saw him did not afford me facilities for making a bacteriologic examination of the discharge from the conjunctiva.

CASE II was that of a medical student who had consulted a doctor on account of gonorrhea, and who, when conjunctivitis was first noticed, had been advised by him to consult me. The urethral trouble had not been bad, and had been carefully treated

from its inception four weeks previously. By that time conjunctivitis had been present for three days; it was sharp, but not severe, nothing like the acuity of an ordinary "gonorrheal conjunctivitis." The swelling of the lids was very moderate indeed, and such discharge as there was, and there was but little, was not at all purulent. The most infected part of the conjunctiva was in the cul de sac, the ocular membrane being almost free of injected vessels; the pain was nothing to speak of. He did not complain spontaneously of joint pains, but these came on almost immediately after the first consultation, and several joints became implicated one after another. In the discharge there were hardly any organisms at all to be found, but the pathologist consulted thought he could make out gonococci in one or two cells, though he was not confident in their aspect, and still more in regard to the quantity in which they were present, they were very unlike the gonococcus.

Five several points in these cases are more or less definitely indicative of the metastatic rather than even an attenuated direct infection, namely: (1) the second patient at least knew clearly the danger of infection and was on his guard from the very beginning; (2) the disease in each case broke out practically simultaneously in the two eyes; (3) the clinical features as regards the secretion, the edema and the severity, were all at variance with what one has observed in cases of conjunctivitis by direct infection; (4) the bacteriologic report is not what is in accordance with such a condition; (5) the fact that the joints were affected at the same time, though it does not of course negative the idea of a direct infection, suggests rather a cause common to joints and eyes having its origin in a generalized infection.

To judge from such of the literature as I have had the opportunity of consulting, this disease seems to be better known to French surgeons than to those of other nations. Indeed, at the discussion of a very interesting paper by van Moll at the International Ophthalmological Congress, in Utrecht (which gives a good résumé of the literature), Morax expressed some astonishment that so very little had been written on the subject outside France; he had himself seen and examined a number of cases. The paper by van Moll illustrates very clearly the great liability to recurrence which the disease displays, for the six cases which he related occurred in the persons of three patients only, in one of whom

there had been two attacks and in another three! They all agreed in the main features with those related above. A point of much interest in the cases as related by a number of surgeons has been the bacteriologic result. In a large proportion of the cases no gonococci whatever have been found in the conjunctival secretion. In point of fact, in a considerable proportion of the cases no organisms of any kind whatever have been found, as is the case also in other forms of conjunctivitis. A suggestion, based on the almost constant presence of staphylococci in cases of metastatic conjunctivitis, has been made that the primary infection of the urethra has been a mixed one of gonococci and staphylococci, that the gonococci had been unable to penetrate the wall of the urethra as the staphylococci had done, and that these latter, making their way into the circulation, had been deposited in joints, causing "rheumatism," and into the conjunctiva and iris. Another and simpler theory is that the eye condition is purely toxic, and in this relation the fact is of great moment that Axenfeld was able to induce a precisely similar condition by introducing into the conjunctival sac a dead culture of gonococci. At all events, there is quite a definite and differentiated form of conjunctivitis, and one which ought to have a place in all good text-books of ophthalmology.

If one looks back to the literature of any branch of medicine some fifty years or more one will find that the idea of metastasis seems to have more attraction for the writers of that day than it has for moderns. In Mackenzie's famous treatise on ophthalmology one finds two classes of gonorrheal ophthalmia spoken of besides the direct infection variety; one of these, which, however, is quite plainly not the condition with which we are at present concerned, is described under the name of "gonorrheal ophthalmia from metastasis." In the days in which Mackenzie lived and wrote his great treatise surgeons seem, whether wisely or unwisely, to have been more disposed to believe in the evil effect of the sudden suppression of a chronic ailment, and especially of the sudden cessation of a chronic discharge, and the cases to which he refers under this heading of ophthalmia from metastasis are in reality examples of acute conjunctivitis from the sudden drying up of a gonorrhea or a gleet. Saint-Yves appears to have been the first surgeon to observe this condition, and his method of treatment

made up in vigor what it may have lacked in wisdom, at least according to modern ideas; he considered that above all things it was necessary in these circumstances to re-establish the flow from the urethral mucous membrane, and the plan adopted was to pass along the urethra bougies smeared with pus either taken from the affected eye or from the penis of another sufferer. As regards the other form of conjunctivitis connected with gonorrhea, spoken of as "gonorrheal ophthalmia without inoculation or metastasis," the evidence of any true or even probable relation between the two was not sufficient to satisfy Mackenzie that the one had anything to do with the other.

Pathology

CIRRHOSIS OF THE LIVER

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Our views concerning the pathology and pathogenesis of cirrhosis of the liver have long been based on the supposition that the liver of man is made up of acini and that the cirrhotic process depends on an interstitial inflammation. In consequence of this, the original opinion of Laennec, that the process was of a neoplastic nature, was completely denied credence, although the correctness of the view that the cirrhotic tissue is newly formed could not be denied at a later date and was accepted *cum grano salis*.

While the older authors, when speaking of cirrhosis, referred only to the small, granular liver, Todd, about the middle of the nineteenth century, recognized the large, granular liver as belonging to the cirrheses, and Hanot, in the seventies, by establishing the biliary hypertrophic form of cirrhosis, included also large, smooth, and hard livers in the conception of the disease. At present it may be said that of the biliary cirrheses only the granular forms, in view of their structure, can be considered among the cirrheses.

In the following remarks, therefore, I shall confine myself to the granular forms of cirrhosis, and shall omit from consideration the smooth icteric liver, since in reality it cannot be said to be cirrhotic. In adopting this division I am in accordance with Frerichs, whose splendid clinical and anatomic descriptions written during the sixties of the last century were of dominating influence, not only for a clear understanding of cirrhosis, but also for that of the normal histology of the liver. It was when the discussion concerning the separation of the multilobular interacinous form from

the monolobular intra-acinous form was inaugurated by Charcot and Gombault that a revision of the older views concerning the pathology of cirrhosis was at all seriously considered; but, despite much work and considerable discussion, little real progress was made. The cause of the relative fruitlessness of the work, a work participated in by a large number of the most prominent histologists, is to be found chiefly in the supposition, formerly generally entertained, that the entire liver is made up of acini; and at that time it would have been difficult, if not impossible, to refer the "granules" found in cirrhosis to changes in supposititious acini—even if this had been taught. Whenever an attempt was made to trace the connective tissue of the cirrhotic liver to the normal periacinous connective tissue, an unexplained incongruence in the histologic picture remained, a fact recognized at the time by a few observers. Charcot, Gombault and others described the "cirrhose biveeneuse;" Ackermann, believing hepatic cirrhosis to be primarily an affection of the parenchyma, considered the disappearance of entire islets of liver tissue to be a part of the process; and Orth correctly recognized and described the vascular remains of acinous structures in the connective tissue.

The description of the histologic picture of hepatic cirrhosis is much simplified if the normal construction of the human liver is understood, whence I venture, at this point, to give a short description of the normal anatomy of the liver.

Hitherto it has been supposed that the normal liver is made up of small lobules, the so-called acini, and it seems probable that the illustrations contained in Frerichs's atlas of the liver are largely responsible for this conception of the liver's construction. These divisions are apparently made out in stained liver sections, but the assumption that they really exist in the human liver is erroneous, and their non-existence can easily be proved by any one making a series of sections. For this purpose, sections made at $\frac{1}{16}$ millimeter intervals suffice to show that in man the normal liver parenchyma is always continuous and connected at the points of junction of the central, lobular, and lobar veins until the vena cava is reached. A description of the histology of the liver, based on the current conception that the central vein forms the center of the acinus, and upon the serial sections, would read thus: The parenchyma of the liver surrounds the hepatic venous tree as a con-

tinuous mantle, while the portal vessels pervade the interstices between the cell mantles surrounding the hepatic venous radicles. This description is morphologically unassailable, but it has the disadvantage of being at variance with the embryologic development of the liver, inasmuch as the columns of hepatic cells develop along the portal ramification into the parenchyma. More akin to this principle is the description of the normal liver structure according to Sabourin, who states that in swine the well developed trabeculae of connective tissue, extending from the periportal connective tissue along the "*veines rectilignaires*" to the central vein, surround the lobule of parenchyma on all sides, and that this area of ramification of a portal radicle, with its accompanying hepatic artery, bile duct, and related columns of hepatic cells with the porto-biliary nodule as a center (the contrary, therefore, of the current description of an acinus, according to which the terminal branch of the hepatic vein is the central vein) has an exact counterpart in the anatomy of the human liver. But this conception of the construction of a lobule, with the porto-biliary nodule as the center, is no more to be maintained for the human liver than the older descriptions, since serial sections show the supposedly periportal hepatic cells to be arranged continuously about the portal vessels, as, according to the former conception, they were thought to be perivenous.

The embryologic analysis, however, which conforms to Sabourin's description, acts as a very good guide to a simple explanation of the arrangement of the parenchyma, as given originally by the anatomist Hyrtl: The portal tree and the hepatic veins, branches of which are constantly crossing each other between the hilum and the vena cava, are so arranged that even the smallest divisions are separated by a layer of parenchymatous cells; and the ramifications of both vascular systems are arranged in a decidedly characteristic manner,—the branches of the portal vein resemble ropes fastened together and form flattened basket-like cups, while the hepatic veins divide in an arborescent manner, the smaller twigs being given off almost at right angles (Figs. 1 and 2).

A comparison of the histologic picture of sections of normal and of cirrhotic livers shows the following differences: In the normal liver the entire parenchyma empties its blood into the central vein

by way of minute venous twigs (*veines rectilignaires* of Sabourin), which are formed by a union of the capillaries. In the cirrhotic liver the parenchyma, aside from the more or less excessive proliferation of the invading connective tissue, shows two striking differences in this respect. At times there are found in the cirrhotic liver portions of parenchyma, the size of a lentil, a pea, or even larger than a bean, which contain distinct hepatic veins; generally there are several of them, but they are irregularly distributed, so that for example four to five central veins, tributaries of a single branch of the hepatic vein, may take up the blood from a nodule of this kind. These pictures represent the type of the old multilobular cirrhosis. By comparison with the appearances found in experimental hypertrophy of the liver (Ponfick) they are easily recognized as rearranged liver tissue the result of regeneration. Furthermore in small islets of liver tissue, eccentrically placed, hepatic veins are found (Fig. 3). Since the surrounding parenchyma is not compressed, these vessels can only have reached this position by an asymmetrical degeneration and regeneration of the parenchyma.

In addition to these vessels, whose relation to the liver parenchyma betrays the fact that they are hepatic veins, there are in cirrhotic livers still larger venous twigs which can generally be injected from the portal vein without special difficulty. Frerichs, therefore, in depicting such a vessel¹ does not figure of it as an hepatic vein. It is to be presumed, however, on account of its central position in a net-work of somewhat tortuous capillaries within a broad band of connective tissue, that he had before him the remains of the vascular skeleton of a lobule in a cirrhotic liver. This lesion in cirrhotic livers was, as far as I know, first correctly interpreted by Orth.² Later, Miura³ described and illustrated these twigs of the hepatic vein within the cirrhotic parenchyma. As the result of investigations carried out in my institute by Koenigstein, I can add that in sections which have been stained for elastic fibers, the connective tissue surrounding such lobular and sublobular veins is characterized by being very poor in elastic tissue (Fig. 4).

¹ Fig. 1, Pl. iii, of vol. ii, of his *Atlas on Diseases of the Liver*.

² *Textbook*, p. 939, Fig. 300.

³ *Tokio Annalen*, vol. iv, p. 49, Pl. iv.



FIG. 1.—Ramification of a normal portal vein.
Macerated and injected preparation. $\times 3$.



FIG. 2.—Ramification of a normal hepatic vein. (Preparation and magnification as in Fig. 1.)



FIG. 3.—Atrophic cirrhosis. Two hepatic veins placed asymmetrically in the hepatic parenchyma, not compressed (no flattening of the columns of cells); bands of connective tissue growing through and partly encircling it. (Apoch. 16 mm., Ocular 4, tube-length 52 cm.)

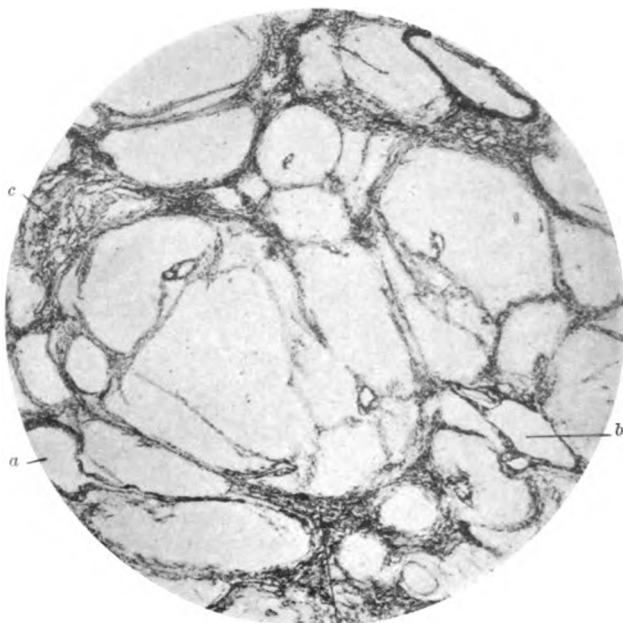


FIG. 4.—Atrophic cirrhosis. Elastic tissue stained; *a*, hepatic vein; *b*, branch of the portal vein; *c*, atrophic area with vestiges of the hepatic veins; *d*, dense connective tissue with new-formed arteries. (Apoch. 70 mm., tube-length 60 cm.)

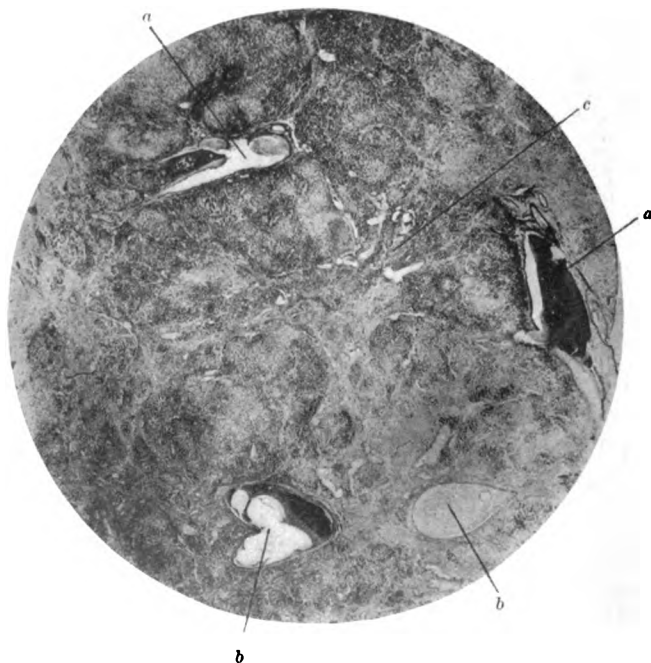


FIG. 5.—Atrophic cirrhosis. Close together near the surface two of the larger branches of the portal and hepatic veins. Lettering as in Fig. 4. (Apoch. 35 mm., Ocular 4, tube-length 52 cm.)

A study of the ramifications of the hepatic veins in the atrophic cirrhotic liver shows, in addition to a mutual approximation of the large branches, corresponding also to the general reduction in the transverse diameter of the mass, a number of areas, approximating acini in size, which are devoid of hepatic veins (Fig. 5). In the coarsely granular cirrhosis (juvenile forms) these areas are generally enclosed by sclerotic connective tissue, not very rich in elastic elements, and the usual net-work of bile ducts. In the irregular, finely granular cirrhotoses, these areas generally contain small and very minute collections of hepatic cells which are completely surrounded, as can easily be shown in serial sections, by connective tissue rich in elastic fibers. The parenchymatous cells in such hepatic tissue sometimes show regressive metamorphosis (Fig. 6); sometimes they are well preserved, or they contain large clear protoplasmic cells. Since in these regions every indication of capillary stasis is lacking, the result cannot be due to a cutting off of a part of an acinus. These isolated groups of cells represent rather regenerated hepatic areas with a peculiar vascularization. If in ordinary atrophic cirrhosis an injection is made from the portal vein, a small part of hepatic tissue is, as a rule, so easily permeated that the injection mass passes over into the hepatic vein at a time when a very considerable part of the parenchyma is still uninjected; more particularly after such injection experiments the large turgescient islets of tissue and the small areas devoid of hepatic veins just referred to remain unaffected. By injecting the hepatic artery, always decidedly enlarged in these cases, these very areas are most easily injected. They may also be partly injected from the portal vein if an injection mass, which passes with greater difficulty, is employed.

Based upon these observations, the circulation in the diseased liver must be depicted somewhat as follows: a small part of the portal blood passes through the remnants of the old acinous channels into the hepatic veins; this passage forms an internal porto-caval anastomosis supplementing the external; to the remaining branches of the portal vein more than the normal amount of arterial blood is furnished; this on the one hand supplies the granular areas of the parenchyma devoid of hepatic veins, and on the other the hypertrophic remains of acinous tissue. This excess of blood passes under increased pressure through the remainder

of the old capillaries, narrowed by atrophy of the acini, and lengthened by hypertrophy of the liver tissue. The lengthening and narrowing of the capillary vessels, and the excess of arterial blood, are the true causes of the increase of portal pressure, as is shown by the occurrence of ascites in subacute atrophy of the liver with regeneration, but without contracting connective tissue.

These changes in the structure of the liver may be very clearly seen in the illustrations of the injected and macerated organ, for which I am indebted to my assistant, Dr. Helly. The portal vein, normally delicate and regular in outline, is dilated, its wall thickened and provided with an increased number of capillaries filled with arterial blood, and its ramifications are more numerous (Fig. 7). The illustration also demonstrates the increased amount of blood in the arterial stream, inasmuch as an isolated preparation of the portal vein into its smallest branches is impossible by injection. Still more striking are the changes in the hepatic veins in the cirrhotic liver (Figs. 8 and 9). The fine ramifications of the venous tree are fewer in number and its larger branches somewhat tortuous; at some points they have attached few, at others many, twisted and tortuous vascular appendages. These appendages represent the sublobular and lobular hepatic veins, which after the atrophy of the parenchyma of the original liver tissue have contracted with it; they correspond to the small distorted vessels in the atrophied parenchyma at *c* of Figs. 4 and 5.

A very instructive preparation is pictured in Fig. 10. The case was one of atrophic cirrhosis, and the illustration shows an injection of the hepatic artery and vein of the lobus Spigelii, which normally is relatively rich in parenchyma cells. The extensive destruction of the hepatic veins of the macerated, injected preparation indicates the advanced stage of the atrophy of the originally normal parenchyma; in spite of this atrophy, the portal branches and the arterial ramifications have been increased in number in consequence of the increase in the supply of arterial blood, and new liver tissue has been produced, which in amount and probably also in functional ability has almost fully replaced the destroyed cells; and just as in the reconstruction and adaptation of a damaged old house stone replaces stone, pillar replaces pillar, so in the reconstruction of the lobe much was changed, the destroyed tissue being replaced in a somewhat changed form layer after layer.

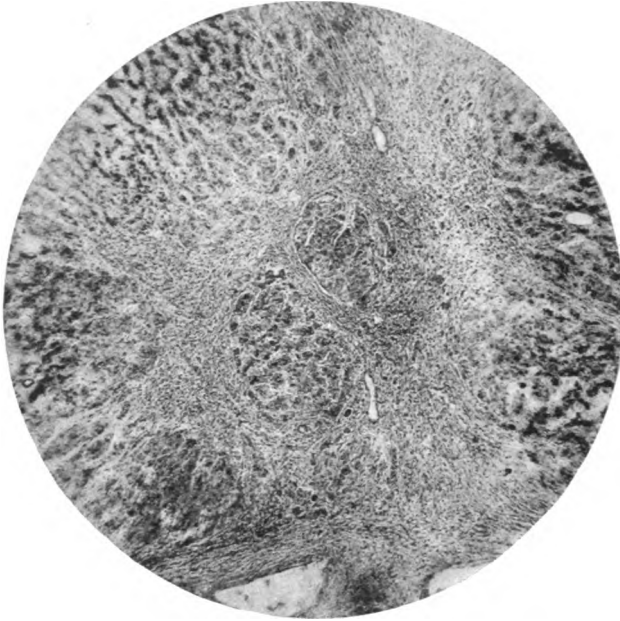


FIG. 6.—Atrophic cirrhosis with ascites and icterus. Pigment atrophy in a part of a "granule" that has no hepatic vein. (Magnification as in Fig. 3.)



FIG. 7.—Portal vein ramifications in atrophic cirrhosis. (Preparation and magnification as in Fig. 1.)



FIGS. 8 and 9.—Ramifications of the hepatic veins in two atrophic cirrhotic livers. (Preparation and magnification as in Fig. 1. Fig. 9 from the same liver as Fig. 7.)

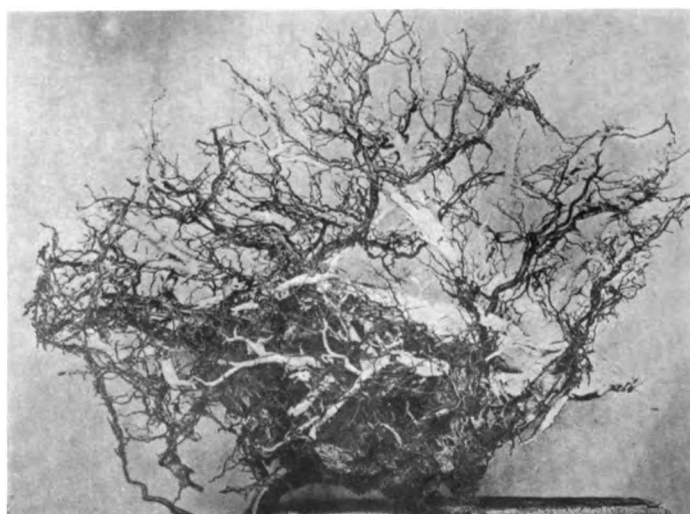


FIG. 10.—Ramifications of the hepatic arteries and hepatic veins in atrophic cirrhosis. Macerated injected preparations; hepatic artery—dark, hepatic vein—light. $\times \frac{5}{4}$.

After studying these extensive changes in the texture of the cirrhotic liver, it is impossible longer to consider the process as a chronic inflammation originating in the interstitial tissues. It is more in accordance with the histologic picture to look upon the process as a deep-seated and complete transformation of the whole parenchyma.

Confirmatory of the view that pathogenetically cirrhosis is a recrudescient, chronic degenerative process of the liver, retarded by ingrowths of regenerating tissue, two additional points seem to me to be of importance. Concerning the first point, I became convinced some time ago, as the result of investigations which Dr. Koenigstein carried out, that the richness in elastic fibers in the newly-formed connective tissue is limited to the zone of the portal-arterial vascular ramification; that on the other hand the bands of connective tissue which accompany the hepatic veins, and especially often the small sublobular veins, presents a tissue free from newly-formed elastic fibers. Since the residual connective tissue following acute atrophy shows the same lack of elastic fibers, the occurrence of numerous elastic elements in chronic cirrhosis is due, I believe, to the fact that the degenerative destruction of newly-formed liver tissue well supplied arterially gives rise to scar tissue rich in elastic elements, an opinion in agreement with the observations of Jores. The sclerosis of an atrophied area and new vascularization following degeneration is not due, as Siegenbeck von Heukelom believes, to a sclerogenesis, peculiar to the cause exciting the degeneration, but rather to their origin from reformed parenchyma, which has probably been totally renewed several times.

The other point worthy of mention is that the beginning of the cirrhotic process is to be sought not in the new growth of connective tissue, but in changes in the parenchyma—an opinion entertained by the older writers, of whom I might mention Frerichs and Ackermann. The transition from the well-known toxic degenerative atrophy of the liver-cells, such as, for example, may easily be observed in experimental alcoholic poisoning, to the beginning of cirrhosis of the liver is to be found in the stage of regenerative hypertrophy. Frerichs⁴ represents such changes in human pathology in his illustrations of fatty and hypertrophic livers; Mertens,

⁴ Atlas I, Pl. 6 and 8.

while inducing cirrhosis experimentally, discovered suddenly in the third week of poisoning numerous mitoses in the hepatic cells of a liver which was not yet cirrhotic. As a further example, I might refer to a human liver (Fig. 11), for a preparation of which I am indebted to Dr. Pilcz. This came from a man 40 years old, who, before his admission to the insane asylum, had used alcohol at times to great excess. He died 4 weeks after his admission. The preparation shows very plainly the intercalation of clear protoplasmic liver-cells in the porto-biliary zones which, according to my belief, is to be regarded as the first regeneration and rearrangement of the hepatic tissue. With this conception of the origin of cirrhosis, the deposits of pigment in the sclerosed connective tissue are also comprehensible (an example of which I gave in a demonstration 4 years ago), as is also the invasion of clear protoplasmic young liver-cells in cirrhosis, to which Adler also recently called attention. These cells represent renewed focal regeneration of the parenchyma after attacks of degeneration (Fig. 12).

With the recognition of cirrhosis as a focal recrudescence, chronic atrophy, modified by the invasion of parenchymatous regeneration, every reason for regarding cirrhosis as a disease entity disappears. The triad, granular liver, enlarged spleen, and portal stasis is as little characteristic of a specific process as stasis and edema are of cardiac insufficiency. Pathology to-day recognizes the cyanotic symptom-complex only as the consequence of the original disease of the valves of the heart, of the heart muscle, of the blood-vessels, or of the lung; similarly the granular cirrhotic liver is in reality nothing more than the result of attacks of degeneration of the liver-cells.

The continually repeated attempts to discover anatomic and clinical criteria for separating the forms of the fully developed hepatic disease do not, therefore, constitute a real advance in our knowledge of cirrhosis; this may be looked for rather in the further search for the causes of degeneration, particularly focal destruction, of the hepatic cells. In addition, the participation of the spleen in the process has been much emphasized in the last few years, on account of the association of alterations in the blood and in the liver-cells, the importance of which is clearly manifested by the frequency of hemosiderosis in the cirrhotic organ.

These changes in our pathologic views are already beginning

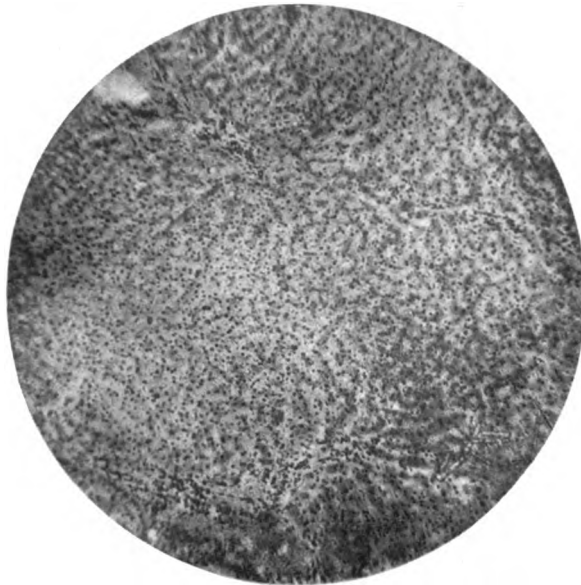


FIG. 11.—Liver of a 40-year old insane patient dying of cirrhosis of the liver and pneumonia. Intercalation of many large liver cells, some of them with double nuclei; bending and distortion of the columns of liver cells and capillaries in the portal zone. (Magnification as in Fig. 3.)

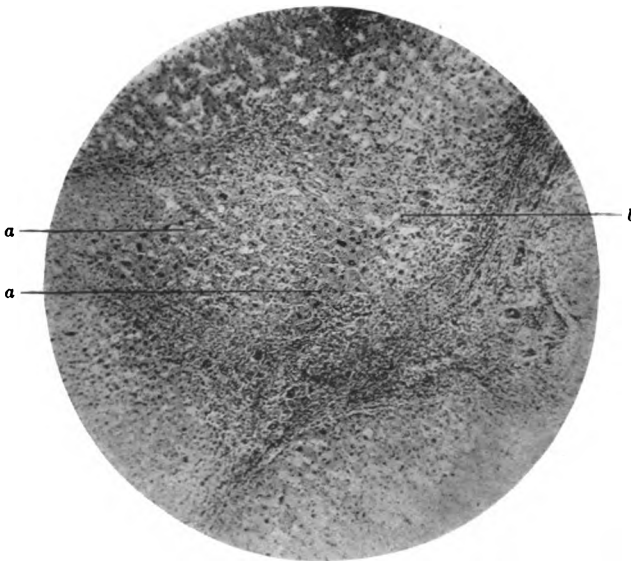


FIG. 12.—Atrophic cirrhosis; death from cancer of the stomach. *a*, focus with large, clear liver cells, rich in chromatin; double nuclei in some of the cells; *b*, dilated capillaries and atrophic liver cells. (Magnification as in Fig. 3.)

to gain ground, especially in the United States, where the knowledge of their existence has been aided and diffused through the exact work of MacCallum; through them the clinician is taught that cirrhosis of the liver in its initial stages, as well as at the onset of grave portal stasis, is still capable of being improved, as under proper conditions the organism has shown great restorative powers. Suitable dietetic treatment promises good results, but they are not to be expected if the physician continues to apply therapeutics indifferently. To be able to determine the proper rational treatment, the results of which, according to the communication of Apert, of Paris, are even apparent to the pathologist, it is necessary to discover at an early period the causes injuring the hepatic cells. The investigation of to-day, from which the best results should be obtained, and which, therefore, have the greatest value from a theoretic and a practical stand-point, are those that pertain to experimental and clinical chemistry.

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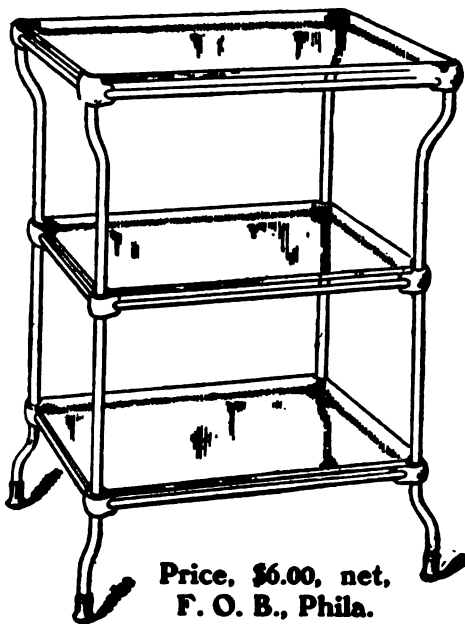
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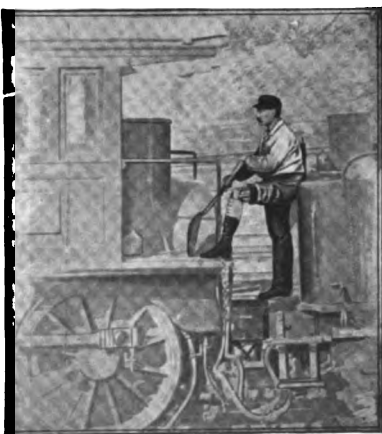
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